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HEIGHT, WEIGHT, AND MORTALITY IN A POPULATION OF LONGSHOREMEN

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INTRODUCTION

RE-EXAMINATION of generally accepted relationships sometimes proves a rewarding form of research. Examination of 5 years of mortality experience in a greatly overweight population of longshoremen has disclosed, surprisingly, no relationship of mortality to overweight. Historically, and even today in certain groups, plumpness has been considered prima facie evidence of good health. The relationship of overweight to high mortality, as now accepted, was brought to light before World War I by the first Medico-Actuarial Mortality Investigation. Further such investigations based on insured male lives have since confirmed this relationship. Some studies not based on life insurance populations have also tended to substantiate these findings of excess mortality among the overweight; still others have not confirmed them. Recently, doubts have been expressed by Keys and others about the relationship of overweight to mortality, and especially about equating overweight with obesity.[1,2]

BASIS OF THE STUDY

In 1951, a multiphasic screening examination (including measurements of height and weight) with diagnostic follow-up, was given to 3,994 longshoremen in the San Francisco Bay Area. Results of this program have been reported elsewhere.[8]

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The 3,994 men comprised about three-fifths of the longshoremen eligible for the examination. The mean annual income of the entire group was about $5,000; the median age of the men examined was 49 years; and about two-thirds of the men examined were basic cargo handlers, performing heavy labor on the docks. They were thus relatively well-paid older manual laborers.

The multiphasic battery included twelve screening tests: height and weight, vision, hearing, chest x-ray, electrocardiogram, blood pressure, serologic test for syphilis, hemoglobin, blood sugar, urine sugar, urine albumin, and medical history.

Of the 3,994 men tested, 2,519 had one or more positive screening tests, and after referral, physicians made positive diagnoses in 1,413 men.

Overweight was screened for referral and a possible diagnosis of obesity. The screening level for overweight was first set at weights 25 per cent above Metropolitan Life Insurance Company's medium-frame standards.* After a very brief period of operation it became obvious that the 25 per cent screening level would result in so many referrals for overweight that the diagnostic follow-up facilities would be overloaded. The screening level was accordingly raised to weights 40 per cent above the Metropolitan standard.

The frequency of obesity diagnoses, even with the screening level set at 40 per cent above standard, was one of the striking findings of the first published report.[8] Also indicated was need for further investigation of the high obesity rates, particularly the relationship of overweight to diagnosed diabetes and hypertensive heart disease which this first study disclosed. Hope was expressed that a weight control program would offer significant benefits to the longshoremen group. A follow-up investigation of mortality in the group through 1956, conducted by the California Department of Public Health, is reported below.

DEFINITIONS, LIMITATIONS, AND ADVANTAGES

Before presenting the findings of this investigation, some definitions of terms, and limitations and advantages of the study should be set out.

The word "obesity" is not used in reporting the findings. Keys[2] has indicated the difficulties in defining and measuring "obesity." "Overweight" in this report means any weight above the mid-point of the "medium frame" range for each height group by Metropolitan Life Insurance Company standards. These standards are well known and widely available, were used in the initial screening, and were used for the analysis of the 1951 screening program.†

The International Statistical Classification of Diseases, Injuries, and Causes of Death uses the term "Arteriosclerotic heart disease, including coronary disease," code 420; subdividing it into "Arteriosclerotic heart disease, so described," code 420.0; "Heart disease specified as involving the coronary arteries," code 420.1; and "Angina pectoris without mention of the coronary arteries,"

*Hereafter referred to as Metropolitan standard.

†Numbers of men by height in inches by weight in ten-pound groups are given for population, total deaths, and coronary heart disease death in Tables V, VI, and VII.

code 420.2. To avoid subdivision, to conform to American usage, and to furnish a convenient term, the words "coronary heart disease" are used throughout to refer to this entire group of diseases.

The relative weight groups used were: (1) 20 per cent and more under Metropolitan standard, (2) 10 to 19 per cent under Metropolitan standard, (3) 9 per cent under to 9 per cent over Metropolitan standard, (4) 10 to 19 per cent over Metropolitan standard, (5) 20 to 29 per cent over Metropolitan standard, (6) 30 to 39 per cent over Metropolitan standard, and (7) 40 per cent and more over Metropolitan standard.

The limitations of this study should be pointed out. (1) This follow-up study has been concerned thus far only with mortality. (2) The study group comprised men in a single occupation group in a single urban area. (3) About 40 per cent of the men in the group eligible for multiphasic examination were not examined. (4) About 4 per cent of the men examined have been lost to follow-up. (5) Only 5 years of follow-up have been done. (6) Only 3,992 persons were studied (height and weight measurements were not made for two of the 3,994 men). (7) Only one measurement of height and weight was made.

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There are advantages to this study also. (1) The group has had complete prepaid medical care available, and further study of morbidity is possible. (2) The study group is homogeneous as to social class and most work-connected variables. (3) The members of one unit (ILWU Local 10) of the group eligible for examination but who were not examined have been studied for mortality; of course, no height and weight measurements are available for this group. Since the latter constituted about four-fifths of the eligible but unexamined group, its experience serves as a check on the bias of participation in the multiphasic screening program. (4) Of the total eligible population, 90 per cent were known to be alive in 1956, 6 per cent were known to be dead, and but 4 per cent have been lost. (5) Enough person-years and deaths have been accumulated to provide sufficient numbers for statistical tests.

METHODS

Five-year follow-up of the study group included checking the union-management welfare fund files, in which current coverage and death benefit payments are recorded; checking membership files of the Kaiser Health Plan, where most longshoremen receive prepaid medical care; and searching the indexes of the California Department of Public Health, which record all California deaths.

In the collation of records of the welfare fund with the original examination records, those men currently covered, whether working or retired, could be classified as still living; those men for whom death benefits had been paid could be classified as dead. The records of the residual who had left the industry, or who had never been covered by the welfare plan, were collated with membership lists of the Kaiser Health Plan, since the latter may cover persons on an individual basis. Those who were under coverage by the Health Plan were classified as still living. Collation of the records of the remainder with the death indexes of the California Department of Public Health disclosed seven deaths in the 5

TABLE I. EXAMINED LONGSHOREMEN BY RESULTS OF MULTIPHASIC EXAMINATION IN 1951, BY AGE AND NUMBER OF DEATHS THROUGH 1956

SCREENING TESTS	ALL AGES[1]				35-44 YEARS			45-54 YEARS			55-64 YEARS			65 YEARS AND OVER		
	EXAMINED	DEATHS	DEATH RATE[2]	LOST TO FOLLOW-UP	EXAMINED	DEATHS	DEATH RATE[2]	EXAMINED	DEATHS	DEATH RATE[2]	EXAMINED	DEATHS	DEATH RATE[2]	EXAMINED	DEATHS	DEATH RATE[2]
Total	3,992	252	12.6	168	1,096	36	6.6	1,384	69	10.0	872	98	22.5	287	47	32.7
Negative—all tests	1,473	32	4.3	70	541	9	3.3	469	11	4.7	197	11	11.2	40	1	5.0
Positive—one or more tests[3]	2,519	220	17.5	98	555	27	9.7	915	58	12.7	675	87	25.8	247	46	37.2
Weight[4]	360	19	10.5	10	103	3	5.8	119	7	11.8	93	5	10.8	25	4	32.0
Only positive test	125	3	4.8	3	46	1	4.3	43	2	9.3	21	—	0	3	—	0
Blood pressure	835	98	23.5	33	174	14	16.1	291	21	14.4	244	38	31.1	105	25	47.6
Blood sugar	156	19	24.3	4	32	4	25.0	53	1	3.8	57	11	38.6	7	2	57.1
Chest x-ray	165	31	37.6	7	28	2	14.3	54	8	29.6	53	14	52.8	23	6	52.1
Electrocardiogram	665	87	26.2	28	129	7	10.9	218	25	22.9	203	31	30.4	87	24	55.2
Hearing	500	51	20.4	25	56	1	3.6	122	7	11.5	193	25	25.9	117	18	30.8
Serologic test for syphilis	412	30	14.6	8	120	6	10.0	178	13	14.6	67	5	14.9	22	6	54.5
Urine albumin	94	23	48.9	1	21	2	19.4	37	11	59.4	20	3	30.0	12	7	116.7
Urine sugar	200	22	22.0	9	34	4	23.5	81	7	17.3	62	10	32.2	11	1	18.2
Vision	947	92	19.4	36	126	5	7.9	384	30	15.6	294	40	27.2	121	17	28.1

From the State of California, Department of Public Health, Bureau of Chronic Diseases.
[1]Includes under 35-year-old group, 353 longshoremen examined, 2 deaths.
[2]Per 1,000 persons per year.
[3]Persons may be positive on more than one test.
[4]Those persons weighing 40 per cent or more over the Metropolitan medium frame standard.

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years searched. The remaining 168 examined men and 88 unexamined men are classified "unable to locate," and are, for the purpose of rate computations, presumed alive. If any of these "unable to locate" men have died in the 5-year follow-up period, they have done so under another name, or after establishing residence in some other state or country.

Death certificates were obtained for all but 8 of the deceased. Those retired to Europe, drowned in Alaska or otherwise deceased, and for whom a death certificate was not obtainable were classified as to cause of death on the basis of the welfare fund records. Classification of the certified deaths follows the International Statistical Classification assigned on the certificate by the Vital Records Section of the California Department of Public Health.

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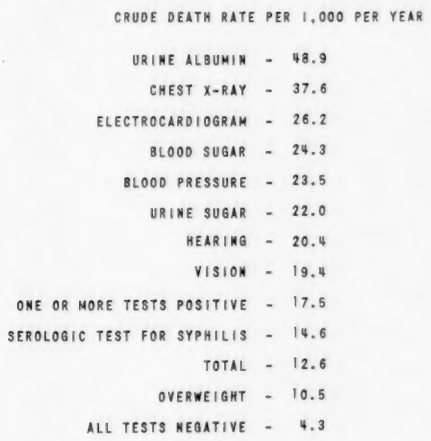
CRUDE DEATH RATE PER 1,000 PER YEAR
URINE ALBUMIN - 48.9
CHEST X-RAY - 37.6
ELECTROCARDIOGRAM - 26.2
BLOOD SUGAR - 24.3
BLOOD PRESSURE - 23.5
URINE SUGAR - 22.0
HEARING - 20.4
VISION - 19.4
ONE OR MORE TESTS POSITIVE - 17.5
SEROLOGIC TEST FOR SYPHILIS - 14.6
TOTAL - 12.6
OVERWEIGHT - 10.5
ALL TESTS NEGATIVE - 4.3

Fig. 1.—Mortality rate by multiphasic findings, longshoremen.

FINDINGS

The follow-up found 3,572 examined men still alive. In the five years, July 1, 1951, to June 30, 1956, following the multiphasic screening, 252 deaths of examined men occurred. Only 168 men, or 4.2 per cent of those examined, have been lost to follow-up. These 168 men did not differ significantly in respect to per cent with positive multiphasic screening findings, nor in respect to per cent with any particular findings, from the total of all men examined. There seems no reason to believe that they are especially subject to mortality, and, in searching the California death indexes, only seven deaths of such men were found.

The findings of the five-year mortality follow-up of the examined group are presented in Table I and in Figs. 1 and 2. In each age group, those having one or more positive screening findings experienced higher mortality than those without positive screening findings. When particular findings are considered, those with a positive urine albumin had the highest mortality, followed by those

with a positive chest x-ray. Then came those with positive electrocardiogram, blood sugar, blood pressure, and the other tests. The 360 longshoremen who were 40 per cent or more overweight had distinctly less mortality than the total of all examined longshoremen, although this extreme overweight group showed higher

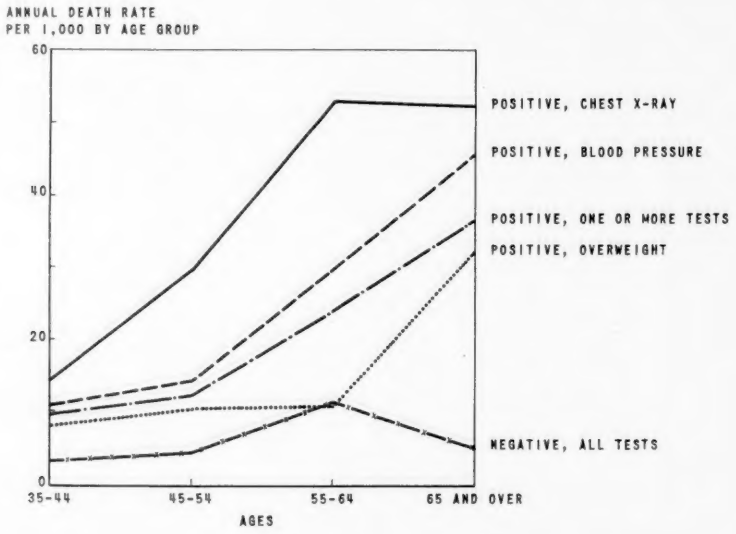

Fig. 2.—Mortality rate by age by multiphasic findings, longshoremen.

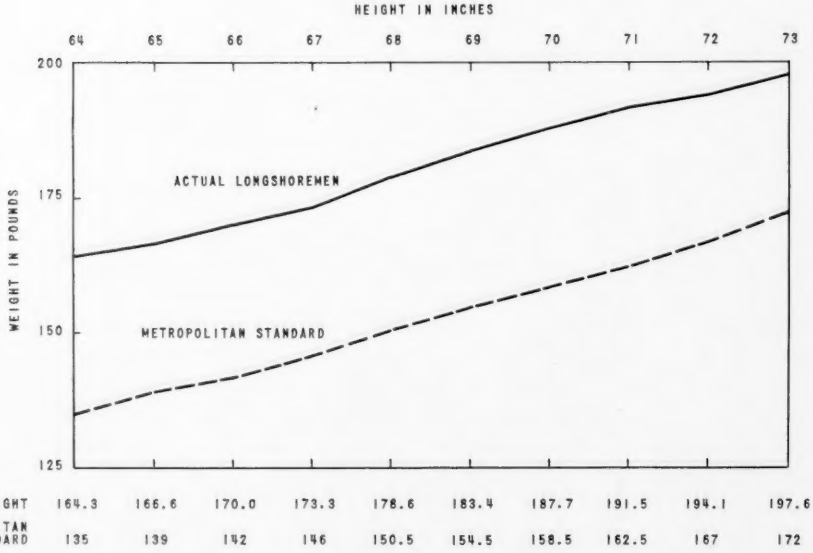

Fig. 3.—Mean weight of longshoremen at each height, 64-73 inches, compared to Metropolitan Insurance Company standards for that height.

mortality than those with no positive finding whatsoever. These relationships are similar for the four age groups. One hundred twenty-five longshoremen showed 40 per cent or more overweight as the only positive finding. Three of these died, a number comparable with the death rates in the negative group, although the numbers are too small for statistical analysis. The unexpected lack of excess mortality in this extreme overweight group led to the analysis of height, weight, and mortality which follows.

WEIGHT GROUPINGS

As Fig. 3 shows, the mean weights of the longshoremen at each height are well above the standard. The relationship of the mean weight at each height to the Metropolitan standard weight for that height is, however, linear. That is, at each height the mean weight of the longshoremen is a relatively constant per cent above the Metropolitan standard, and the distributions of weights around this mean are similar. For the range of heights from 64 to 73 inches, for which there are more than 100 longshoremen at each height, the mean weights are about 17 per cent above Metropolitan standard. Men of various heights can thus be considered simultaneously by grouping according to the variation of their weight from the standard. Height is thus eliminated as a separate variable, and the weight relative to Metropolitan standard is used.

Age cannot be eliminated as a variable. It is correlated with weight group and, of course, with mortality. Tables II and III show that the longshoremen under 35 years of age are, on the average, less over the standard weight than all men examined. Those 75 years and over are, likewise, lighter. Within the age range 35 to 74, the distribution of weight by age is sufficiently constant to allow summations over age. This summation is used in Table IV to allow a subdivision by cause of death.

MORTALITY BY WEIGHT GROUP

The distribution of men and of deaths by age group and weight group is shown in Table II. Dividing the number of deaths in each age-weight class by the number of persons in that class yields the detailed death rates also shown in Table II.

The rates shown in Table II do not differ significantly from one weight group to another.* There is no gradient whatsoever toward higher mortality in the more overweight classes. This is the central finding of the present study. The following sections present other data bearing on this central finding.

Table IV shows mortality by cause group by weight class for longshoremen aged 35 to 74. The mean per cent overweight of those deceased of coronary heart disease does not differ significantly from the mean of all deceased, nor from the means of the four age groups of deaths. Obviously, then, the coronary heart disease deaths are not concentrated in the most overweight groups of the examined population.

*A statistical test made by computing expected numbers in each class, combining those at or below the standard weight, and combining over age, resulted in a chi square far below the value required for statistical significance at the 0.05 level.

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Those dying of other cardiovascular conditions had a significantly higher mean weight, which, when analyzed by specific cause groups, proved to be most characteristic of cerebrovascular accident deaths, at older ages, and of deaths attributed to heart diseases other than hypertensive or coronary. Those who,

TABLE II. NUMBER OF LONGSHOREMEN EXAMINED, DEATHS IN FIVE YEARS AND AGE-SPECIFIC MORTALITY RATES BY WEIGHT CLASS AND AGE GROUP

WEIGHT CLASS[1]	ALL AGES	UNDER 35	35–44	45–54	55–64	65–74	75 AND OVER
	Population						
All weights	3,992	353	1,096	1,383	873	276	11
20 per cent under	6	0	2	1	1	2	0
10-19 per cent under	80	12	16	24	19	9	0
±9 per cent	1,176	142	342	411	209	67	5
10-19 per cent over	1,011	88	273	358	220	70	2
20-29 per cent over	864	67	237	292	206	59	3
30-39 per cent over	495	24	123	178	125	44	1
40 per cent and more over	360	20	103	119	93	25	0
	Deaths						
All weights	252	2	36	69	98	45	2
20 per cent under	1	0	0	0	0	1	0
10-19 per cent under	10	0	0	3	5	2	0
±9 per cent	66	2	15	17	25	6	1
10-19 per cent over	72	0	5	21	31	14	1
20-29 per cent over	57	0	9	16	22	10	0
30-39 per cent over	27	0	4	5	10	8	0
40 per cent and more over	19	0	3	7	5	4	0
	Death Rates[2]						
	Crude Rate	Adjusted Rate[3]					
All weights	12.63	12.63	1.1	6.6	10.0	22.4	32.0	A
20 per cent under	B	B	A	A	A	A	A	A
10-19 per cent under	B	B	A	A	25.0	52.6	A	A
±9 per cent	12.2[B]	13.4[B]	2.8	8.8	8.3	23.9	17.9	A
10-19 per cent over	14.2	14.4	0	3.7	11.7	28.2	40.0	A
20-29 per cent over	13.2	13.0	0	7.6	10.9	21.3	33.9	A
30-39 per cent over	10.9	10.0	0	6.5	5.6	16.0	36.4	A
40 per cent and more over	10.6	10.0	0	5.8	11.8	10.7	32.0	A

From the State of California, Department of Public Health, Bureau of Chronic Diseases.

[1]By Metropolitan medium frame standard.

[2]Rates are per 1,000 persons per year.

[3]Adjusted to the total longshoremen population by the indirect method.

A—Rates not computed on fewer than 19 persons.

B—Death Rate for combined group at and under standard.

after having been diagnosed as having coronary disease at the time of original examination, died of other cardiovascular causes, had a mean weight 15 per cent above standard. This mean weight did not differ from that of persons whose deaths were coded coronary.

TABLE III. MEAN PER CENT OVER METROPOLITAN MEDIUM FRAME STANDARD FOR ALL EXAMINED LONGSHOREMEN AND FOR THOSE DEAD IN 5 YEARS BY AGE GROUP

	ALL AGES	UNDER 35	35–44	45–54	55–64	65–74	75 AND OVER
All examined—number	3,992	353	1,096	1,383	873	276	11
Mean[1]	17.3%	12.8%	17.0%	17.3%	19.2%	18.1%	12.7%
Standard deviation	15.2%	—	—	—	—	—	—
Dead in 5 years—number	252	2	36	69	98	45	2
Mean[1]	16.4%	A	16.0%	16.8%	15.5%	19.3%	A

From the State of California, Department of Public Health, Bureau of Chronic Diseases.
[1]Per cent over Metropolitan medium frame standard.
A—Numbers too small for calculation of mean.

TABLE IV. TOTAL DEATHS OF EXAMINED LONGSHOREMEN, AGES 35-74 YEARS, BY CAUSE GROUP BY WEIGHT CLASS, 5-YEAR EXPERIENCE, 1951-1956

WEIGHT CLASS[1]	TOTAL	CAUSE OF DEATH				
		CARDIOVASCULAR DISEASE		CANCER	ACCIDENTS, POISONING, AND VIOLENCE	OTHER
		CORONARY HEART DISEASE	OTHER			
All weights	248	78	39	53	25	53
20 per cent under	1	0	0	0	0	1
10-19 per cent under	10	3	1	4	0	2
±9 per cent	63	20	7	19	5	12
10-19 per cent over	71	22	8	19	10	12
20-29 per cent over	57	17	14	7	5	14
30-39 per cent over	27	9	6	2	1	9
40 per cent and more over	19	7	3	2	4	3
Mean[2]	16.6%	17.2%	20.5%	10.6%	19.6%	17.5%

From the State of California, Department of Public Health, Bureau of Chronic Diseases.
[1]By Metropolitan medium frame standard.
[2]Per cent over Metropolitan medium frame standard.

POSSIBLE INFLUENCE OF SELECTION ON EXPERIENCE OF THE EXAMINED GROUP

The frequency of coronary heart disease deaths in the examined population was low in comparison with the coronary heart disease death rates for California males, 1951-1956. Application of the 1954 rates to the examined longshoremen

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population aged 35 to 74, by 5-year age groups—allowing for the 5 years of aging in the population and for attrition by death—gives an expected number of 119 coronary heart disease deaths, more than three standard deviations above the observed number of 78 deaths. Thus, the examined longshoremen show a standardized mortality ratio for coronary heart disease of 66 (where the standard is 100). The total number of deaths expected from all causes was 316 compared to the observed number of 252. This yields a standardized mortality ratio of 80. Hence, the examined longshoremen appear to have experienced a significantly lower mortality from all causes in the 5-year follow-up period than would be expected from their age distribution. Their mortality from coronary heart disease was particularly below expectation. These low mortalities occurred in spite of the great amount of overweight among this population.

TABLE V. HEIGHT AND WEIGHT OF LONGSHOREMEN POPULATION AT TIME OF EXAMINATION IN 1951. NUMBER OF MEN

WEIGHT POUNDS	TOTAL	HEIGHT—INCHES													
		60 AND UNDER	61	62	63	64	65	66	67	68	69	70	71	72	73 AND OVER
Total	3,992	4	8	25	74	136	299	406	546	674	619	463	344	201	193
240 and over	96			1		1	1	2	3	9	13	22	16	7	21
230-239	69					1		2	5	7	20	5	13	8	8
220-229	134						2	2	13	12	17	30	21	17	20
210-219	202					2	6	10	22	35	36	23	24	20	24
200-209	309				1	2	12	16	25	58	54	43	40	27	30
190-199	442	1		1	3	11	21	36	51	73	84	62	45	28	26
180-189	610		1	1	5	12	34	58	81	115	105	84	62	29	23
170-179	600		1	4	8	18	45	66	86	105	98	68	52	30	19
160-169	590		1	3	9	27	63	76	92	105	76	74	29	21	14
150-159	465			5	20	27	41	68	80	89	64	29	28	10	4
140-149	283		2	5	10	13	46	40	53	47	37	14	10	4	2
130-139	139	1		2	11	19	19	23	23	15	14	8	2		2
120-129	42		3	2	5	3	6	6	10	4	1	1	1		
110-119	9	1		1	2		2	1	2						
Under 110	2	1					1								

From the State of California, Department of Public Health, Bureau of Chronic Diseases.

This finding was not in agreement with findings from another California study, yet unpublished. This was a study of mortality by occupation for California, 1949-1951, using the census population counts and the occupations stated on death certificates. It showed a coronary heart disease mortality ratio of 108 for longshoremen, in contrast to the ratio of 66 among those who had multiphasic screening. The higher ratio, of course, is based on all longshoremen in California, estimated at 9,658 persons between 20 and 64 years of age, of which the population eligible for examination comprised about two-thirds. The census population

study indicated a total mortality ratio for California longshoremen 1949-1951 of 134, in contrast to the mortality ratio of 80 in the examined population reported here. These conflicting findings have been somewhat resolved by studying the group eligible for examination but not examined in 1951, and by closer investigation of those reported as longshoremen from the San Francisco Bay Area on their death certificate statement of occupation.

TABLE VI. HEIGHT AND WEIGHT OF EXAMINED LONGSHOREMEN WHO DIED BETWEEN 1951-1956. NUMBER OF DEATHS

WEIGHT POUNDS	TOTAL	HEIGHT—INCHES													
		60 AND UNDER	61	62	63	64	65	66	67	68	69	70	71	72	73 AND OVER
Total	252	0	1	3	12	10	30	30	32	46	39	20	14	9	6
240 and over	6									1			1	1	3
230-239	6							1			2	1	2		
220-229	4									2			2		
210-219	10							1		2	3	1	1		2
200-209	16						1		1	3	3	3	3	2	
190-199	30					1	1	3	5	5	5	4	2	3	1
180-189	31						2	3	5	9	5	4	1	2	
170-179	36					2	6	3	5	10	5	3	1	1	
160-169	35				1	4	6	5	7	4	6	2			
150-159	32				5		5	6	2	8	5		1		
140-149	19				1	2	6	3	3	1	1	2			
130-139	15			1	3		1	3	3		4				
120-129	10		1	2	1	1	1	2	1	1					
110-119	1				1										
Under 110	1						1								

From the State of California, Department of Public Health, Bureau of Chronic Diseases.

The unexamined group of ILWU members was studied by reconstructing the ILWU-PMA welfare fund eligible list for Local 10 (San Francisco) as of July 1, 1951, and following the unexamined men on this list through the same methods described above. The Local 10 members were about four-fifths of the longshoremen in the San Francisco Bay Area. The results of this follow-up are presented in Table VIII. There was no significant difference in age distribution between examined and unexamined, the mean age of the examined being 49.1 years, of the unexamined 48.9, and the percentages at each age being very similar. Thus, the significant differences in mortality and in cause of death reported below cannot be due to age differences.

The annual death rate per thousand from all causes, adjusted for aging and for attrition due to death, was 13.0 for the examined men, and 20.8 for the unexamined, 1.6 times as high. This indicates a standardized mortality ratio of 128 for the unexamined longshoremen, comparable to the ratio of 134 found for

the total California longshoremen population by the census-occupation study. That this higher mortality for unexamined men is partially due to initial selection for health level is indicated by the slight rise in mortality for the examined group and the slight drop in mortality for the unexamined group from the first to the second year after examination. That something else is operative is indicated by a continued difference at a ratio about 1.6 to 1 for the fourth and fifth years of follow-up. The cause-specific mortality differences are greatest for cancer, where the unexamined show more than twice the mortality of the examined. These differences are least for cardiovascular conditions other than coronary heart disease, where the unexamined show only about a 1.2 to 1 ratio. Summing the unexamined and the examined, however, the entire group of eligibles for examination reveal a standardized mortality ratio of only 95, whereas the census-occupation study indicated a ratio of 134.

TABLE VII. HEIGHT AND WEIGHT OF EXAMINED LONGSHOREMEN WHO DIED BETWEEN 1951-1956 FROM CORONARY HEART DISEASE. NUMBER OF DEATHS

WEIGHT POUNDS	TOTAL	HEIGHT—INCHES													
		60 AND UNDER	61	62	63	64	65	66	67	68	69	70	71	72	73 AND OVER
Total	78	0	0	1	2	2	7	10	12	15	14	7	4	2	2
240 and over	2												1		1
230-239	3										2		1		
220-229	2									1			1		
210-219	4									2	1				1
200-209	6								1		2	2		1	
190-199	10							1	1	2	3	2		1	
180-189	7								2	3	1		1		
170-179	10						2	1	2	3	1	1			
160-169	14						2	2	4	2	2	2			
150-159	5				1			2		2					
140-149	7					1	2	3	1						
130-139	5				1			1	1		2				
120-129	3			1		1	1								
110-119	0														
Under 110	0														

From the State of California, Department of Public Health, Bureau of Chronic Diseases.

Next, those deaths in the second half of 1951 reported on death certificates as longshoremen from the San Francisco Bay Area were studied. The census-occupation study revealed 35 longshoremen deaths during the second half of 1951, the period of overlap with the present study. Of these, 24 were in the eligible group, 12 examined and 12 not examined. The remaining 11 were not in the eligible group. Further analysis indicates that, since 7 of these 11 ineligibles were known to the union as former or part-time members, a separation into three categories should be made.

TABLE VIII. NUMBER OF EXAMINED AND UNEXAMINED LONGSHOREMEN BY AGE AND BY CAUSE AND DATE OF DEATH

	AGE GROUP						
	TOTAL	UNDER 35	34–44	45–54	55–64	65–74	75 AND OVER
	Population						
Examined							
Total number	3,992	353	1,096	1,383	873	276	11
Per cent of total	100.0%	8.8%	27.5%	34.6%	21.9%	6.9%	0.3%
Mean age (years)	49.1						
Unexamined							
Total number	1,665	167	480	528	351	134	5
Per cent of total	100.0%	10.0%	28.8%	31.7%	21.1%	8.1%	0.3%
Mean age (years)	48.9						
	Deaths by Cause						
	NUMBER	DEATH RATE*					
Examined							
Total	252	13.02	2	36	69	98	45	2
CV coronary	78	4.03	–	10	19	35	14	–
D other	40	2.06	–	5	5	16	13	1
Cancer	54	2.80	1	4	12	30	7	–
Violence	25	1.29	–	6	12	5	2	–
All other	55	2.85	1	11	21	12	9	1
Unexamined							
Total	165	20.84	3	13	41	64	43	1
CV coronary	43	5.44	2	3	11	15	12	–
D other	19	2.40	–	—	5	5	9	–
Cancer	52	6.57	–	3	8	28	12	1
Violence	19	2.40	–	5	9	4	1	–
All other	32	4.04	1	2	8	12	9	–

	Date of Death											
	EXAMINED						UNEXAMINED					
	TOTAL	1951-1952	1952-1953	1953-1954	1954-1955	1955-1956	TOTAL	1951-1952	1952-1953	1953-1954	1954-1955	1955-1956
Total number	252	37	49	54	54	58	165	35	29	30	38	33
Annual death rate	13.02	9.3	12.5	13.9	14.1	15.4	20.84	21.2	18.0	18.9	24.5	21.8
CV coronary	78	12	9	14	21	22	43	7	8	9	8	11
D other	40	5	10	9	8	8	19	1	6	4	5	3
Cancer	54	8	14	12	12	8	52	16	10	10	9	7
Violence	25	7	7	7	2	2	19	5	2	2	6	4
All other	55	5	9	12	11	18	32	6	3	5	10	8

From the State of California, Department of Public Health, Bureau of Chronic Diseases.

*Annual Death Rate per thousand. Differs from Tables I and II because these rates have been adjusted for drop out of deaths, which differs between examined and unexamined.

1. Union members in good standing, who worked 800 hours or more in 1950 (eligibility requirement) and who were working regularly in the summer of 1951 (examination exposure), and who reported for multiphasic examination. This defines the examined group.

2. Union members in good standing, who worked 800 hours or more in 1950 (eligibility requirement) but who, (a) were not working regularly at longshoring in the summer of 1951 (unexposed to examination) or, (b) for other reasons did not participate in the multiphasic screening program (resistant to examination). This defines the unexamined eligibles.

3. Union members who had not worked 800 hours in 1951, or who were not in good standing, plus nonmembers who may have had union work permits and who obtained casual jobs on extra gangs. This defines those ineligible for the multiphasic screening but who may be called longshoremen on their death certificate.

The examined group would be expected to show less mortality than the other two (unexamined) groups for the first year or so, since eligibles who were not working regularly because of illness would be unexposed to examination. Table VIII indicates that this is especially true for cancer deaths.

An analysis of the 11 ineligibles dying in the second half of 1951 showed that 5 of them died of alcoholism or cirrhosis of the liver. None of the eligibles died of these causes in this period. This seems to imply that persons in the final stages of alcoholism are overrepresented in the ineligible group, which implication, from the definition of the group, seems reasonable. The mortality ratio among alcoholics is about 250, and, as a very rough estimate, a mortality ratio of 250 among ineligibles may be assumed. To produce a total ratio of 130 among all longshoremen, then, would require 4,000 with a ratio of about 80 (the examined), 1,600 with a ratio of about 130 (the unexamined), and 800 with a ratio of about 250 (the ineligibles). This number, 800, seems in reasonable agreement with the number of persons in the areas along the waterfront in which such casuals may live.

This analysis of mortality experience among the unexamined and among those called longshoremen but not eligible indicates that the examined group was selected, as any examined group always is. However, the analysis does not suggest that overweight-coronary-prones tended to avoid examination. Thus selection of the examined group does not appear to have influenced the central finding of the present study.

INCIDENTAL FINDINGS

Excesses of mortality, from all causes, from heart disease specified as involving the coronary arteries (420.1), and from cancer, occurred among those men who usually smoked a pack of cigarettes per day or more, as compared with men who smoked less or not at all. The excess of coronary deaths was more pronounced in men under 55. No significant excesses were observable in arteriosclerotic heart disease so described (420.0), other cardiovascular disease, accidents,

or all other causes. These findings will be presented in detail later, after additional years of follow-up.

Another peripheral finding of some interest, shown in Table IV, is that those destined to die of cancer had a mean weight only 10.6 per cent above the standard as compared with a mean for those 35 to 74 years of age of 16.6 per cent above the standard. The weight at time of multiphasic screening may well have been reduced by undiagnosed disease, but Reed and Love[7] have also reported that those who were to die of cancer were distinctly below average in weight.

Another finding is the relatively small proportion of the coronary heart disease deaths in which a diagnosis of coronary heart disease was made as a result of referral from the screening examination. Of the 78 deaths coded to coronary heart disease, only 12 were diagnosed as a result of the multiphasic examination. Of the 142 longshoremen diagnosed coronary heart disease after referral from the screening examination, 28 died, 12 of coronary heart disease; 6 were lost to follow-up; and 108 were still alive after 5 years.

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DISCUSSION

Several possible explanations can be offered for the observed lack of association between overweight and excess mortality. Some explanations arise from the study's limitations. The unexamined may possibly have had an extremely different weight distribution from those examined. There remains the remote possibility that the 4 per cent lost to follow-up had an extremely different mortality. The period of follow-up may have been too short for excess mortality to have developed among the overweights, but time will remedy this possible defect in the study.

The muscularity of the longshoremen, due to the heavy labor of their work, is commonly advanced as explaining both their overweight and their relative good health. However, most men more than 40 per cent above the standard weight are probably carrying a substantial amount of fat. One must also consider the possible salutary effect of physical activity suggested by Morris.[6]

Explanations of another sort rest upon the idea that occupational selection tends to keep the fat man with high mortality risk out of the group studied. Heavy work may repel this type of overweight person, and he may go into white-collar occupations. Or, once his health begins to deteriorate, he may leave longshore work.

Still other explanations are possible. The older longshoremen are largely foreign-born and may have European, rather than American, patterns of mortality. Many of the younger longshoremen are Negroes, and still other patterns may apply. About one-third were in some work classification other than basic cargo handler, although no differences in per cent of deaths appear by work classification. Any of these differences may have had some effect on the group's mortality experience.

However, the most plausible explanation appears to be that the usual relationship of overweight to excess mortality does not hold for all groups, particularly for the longshoremen studied and reported here.

SUMMARY

The 3,992 examined longshoremen, averaging 17 per cent over Metropolitan standard of weight for height, show no excess of mortality from all causes and no excess from coronary heart disease during the first 5 years after examination. They show no gradient of total mortality with weight, even those 40 per cent and more over Metropolitan standard of weight for height showing no excess mortality. The 78 examined longshoremen who died of coronary heart disease in the 5 years after examination did not differ in weight from the total of those examined. Only 12 of the 78 coronary heart deaths occurred among those diagnosed as having coronary heart disease after referral for positive findings at the multiphasic screening examination.

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STATISTICAL COMPARISON OF METHODS TO EVALUATE ANALGETICS

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THE evaluation of analgetic agents in humans is a continuing problem which has no "classical" solution. Investigators are constantly seeking methods to increase precision of the potency comparisons and yet remain within the bounds of practical expedience. All agree that some statistically sound procedure is required. A frequently used method is one in which each patient acts as his own control; that is, each patient receives all of the agents in the study. This method is here compared with one in which each patient received one drug only. In post-partum pain studies, the latter approach seems to have several advantages, which are discussed in this paper. There is reason to believe that these advantages may have application in other areas of clinical experimentation.

A full clinical report of the data used in this paper was recently published by Peeters.[1] A brief summary of the experimental method is included here to orient the reader.

METHOD

The study was done with a new synthetic analgetic agent, dextromoramide.* Animal pharmacologic[2,3] and preliminary clinical[4,5] studies have indicated that this is a potent and relatively nontoxic analgetic agent. During a four-month period 307 women were delivered and subsequently observed for at least one week at the Maternity Hospital in Turnhout, Belgium. Of these, 107 eventually complained of a syndrome diagnosed as typical afterpain and asked the physician in charge of the ward to do something about it. From this group, 87 sufficiently intelligent, cooperative mothers judged to have "severe" pain were selected for study. All patients were unaware of the fact that they were the object of special study.

Boxes containing four suppositories, coded as to patient and order of administration, were assigned to each mother. The four suppositories in each box contained, respectively, 20, 10, or 5 mg. of dextromoramide or 1,300 mg. of excipiens (placebo). The four suppositories were randomly arranged in the boxes. Such

*1 *d*-l-(β-Methyl-α, α -diphenyl -4-morpholinebutyryl) pyrrolidine.

packaging and coding helped to assure that double-blind conditions would be maintained.

The study was supervised by four staff physicians. The same doctor answered all calls from any one mother. The first suppository was given at the mother's request for post-partum pain relief. The other assigned suppositories were given at the time of the mother's spontaneous complaints about severe or "unbearable" afterpains. The interval between two successive doses was restricted to two or more hours. No other drug was administered during the test periods.

Each time a new suppository was administered the patient was interviewed by her attending physician. All possible information concerning the previous dose—as far as possible in the patient's own words—was recorded on special forms. Care was taken to avoid asking suggestive questions and showing unusual interest.

Each day the notes were reviewed by the investigator and the attending physician, and the degree of pain relief obtained for each dose was evaluated by interpretation of the patient's statements. The results were expressed as *no relief*, *partial relief*, and *complete relief*. In setting up the study, complete relief was defined as relief of pain within 30 minutes following administration, lasting for at least 3 hours. Where possible, the duration of relief was also recorded.

For this paper, only two categories of relief are used: *complete relief* and *inadequate relief*. When results did not meet the criteria for complete relief, they were considered as inadequate relief.

RESULTS

In a study such as this all patients are not expected to require a drug four times for relief of pain. The drug requirements of the patients in this study are shown in Table I.

TABLE I. SUPPOSITORIES ADMINISTERED FOR AFTERPAIN RELIEF

NO. SUPPOSITORIES PER PATIENT	NO. OF PATIENTS	TOTAL SUPPOSITORIES
1	24	24
2	20	40
3	16	48
4 or more	27	123
Total	87	235

Since there were four different doses in this study, the most frequently used statistical analysis of the results would include only the 27 patients who were given all four drugs. Thus only 108 (4×27) suppositories out of 235 given would be included in the calculations.

A second valid statistical analysis would be based upon a tabulation of all first doses. This would include the results of only 87 suppositories. If the response to a given dose is the same regardless of previous treatment and hours

post-partum, the results of these two approaches are equivalent and the results of all drugs given could be pooled for an over-all summary of results. However, if the results from the first dose differ from the results when all four doses are given, there is little justification for pooling data from patients for whom all drug comparisons are not available.

Thus the evaluation of this experimental approach depends upon a comparison of first doses versus all four doses. These results are tabulated in Table II and illustrated in Fig. 1. The results of all doses after the first one are also listed.

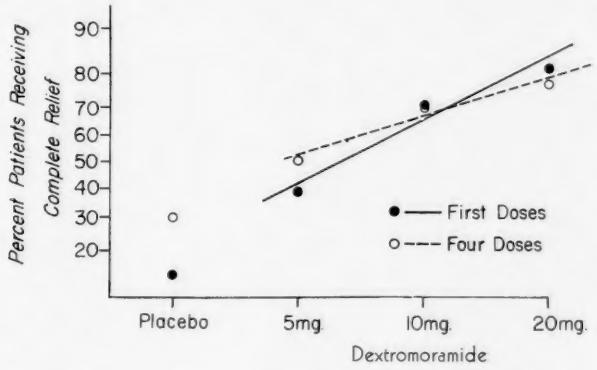

Fig. 1.—Results of first doses compared with results of total doses.

TABLE II. DOSES GIVING COMPLETE RELIEF OF AFTERPAIN

	NO. OF DOSES	PLACEBO	5 MG.	10 MG.	20 MG.
First doses only	87	3/21 = 14%	9/23 = 39%	15/21 = 71%	18/22 = 82%
All doses after the first one	148	12/36 = 33%	22/35 = 63%	29/40 = 72%	30/37 = 81%
Total	235	26%	54%	72%	81%
Patients who received all drugs	108	8/27 = 30%	14/27 = 52%	19/27 = 70%	21/27 = 78%

The results of the first doses are more sensitive to drug potency changes. The placebo response is smaller, suggesting that on the first dose patients may have greater need for relief and thus can better discriminate between drug and placebo. The graph of the best-fitting straight lines clearly shows a steeper slope over the dose range studied. Table II shows how the response to the first doses is diluted by the addition of subsequent administrations.

Statistically speaking, the more desirable evaluation procedure would be the one with the steeper slope for the dose response lines demonstrated in Fig. 1. This increased precision insures more accurate comparisons between drugs when different compounds are studied. Steep slopes can also be looked upon as a way

to reduce the number of observations required to carry out an analgesic study. The precision of this type of assay procedure is approximately proportional to the slope and to the square root of the number of observations used.[6]

A quantitative comparison of the two approaches can be made by estimating the standard error of the ED_{50} for each method. The calculations are as follows:

Probit slope for first doses = 0.60641, 87 observations
Probit slope for four doses = 0.36454, 108 observations

$$\text{Approximate standard error for } ED_{50} = \frac{1}{\text{slope}}\left[\frac{2}{\text{(no. of observations)}}\right]$$

$$= 0.250 \text{ for first doses}$$
$$= 0.373 \text{ for four doses}$$

Of course, the smaller standard error indicates the more precise procedure. Another way to express this would be a comparison of sample sizes required. With the data above, it can be shown that the four dose per patient analysis would require 240 observations on 60 patients to give precision equivalent to that already available from the 87 first doses.

Since most human pharmacology techniques must also consider side effects, it should be noted that the comments on evaluation of efficacy also apply to side effects. Table III shows that the side effects observed for the first dose administered are similar to the results found when all drugs were given to the 27 patients.

TABLE III. INCIDENCE OF SIDE EFFECTS OBSERVED

	PLACEBO	5 MG.	10 MG.	20 MG.
First doses only	0/21	0/23	2/21	5/22
All doses after the first one	1/36	1/35	3/40	8/37
Patients who received all drugs	1/27	0/27	1/27	7/27

DISCUSSION

These results indicate that the most efficient estimate of drug potency can be determined from the effects of the first drug administered. The term "efficient" is intended to include an improvement in precision, use of all data collected, and a simple, practical, and expedient study plan requiring a minimum of dosage instructions. Observing only first doses given to patients with severe pain guarantees that all data taken can be used in the final calculations. This may also have administrative advantages in that patients will require special attention for a much shorter period of time. Certainly more patients could be studied with less total effort expended.

Extending this argument to the data at hand, it would require a study of approximately 200 patients to acquire 60 patients who used at least four drug doses. The summary of these 240 (4×60) doses would be equivalent, in precision, to the results for the 87 first doses reported above. Actually, the dose response line for all doses in this study is not as precise as the line for the 87 first doses.

Precision is emphasized here, for experimental techniques like this will be employed to measure differences between two or more analgetic agents. Subtle differences can be detected only by efficient methods or very large samples. Present-day requirements rarely permit large studies.

The assignment of one drug to a patient can have additional advantages. It would be possible, for example, to consider the average number of drug doses needed to provide adequate relief for 24 hours or, perhaps, throughout the full period of pain. This would be a practical as well as meaningful index of efficacy. Such an approach would no doubt apply to comparisons of drugs in which a placebo was not required.

On occasions, drugs are studied in which one of the agents is a potentiator.[7] When all drugs are given to the same patient, some orders of administration will have hidden potentiating effects. If potentiation is not anticipated, the results can be misleading. One drug per patient will avoid this dilemma.

It is not uncommon to find patients who do not respond to the particular agent under study. In this situation, giving several graded doses of one compound may bring about complications in the hospital routine as well as presenting incomplete or questionable data for evaluation. The use of first doses only will avoid such complications.

The text of this paper suggests that the magnitude of the placebo response might be used as an index of sensitivity. Although this may be true for postpartum pain where the discomfort and psychologic elements differ from the more stressful experiences of postoperative and chronic pain, it has not yet been established that such a relationship holds for all types of pain. In fact, Lasagna[8] has shown that placebo relief is inversely related to the number of doses given. Beecher[9] has shown that it is very difficult to distinguish between placebo and morphine when studying first doses for postoperative pain.

Certainly test methods using only first doses will require further study with other compounds. However, the evidence presented here indicates that future work in this direction should be encouraged. Experimental techniques for human research which will reduce the number of subjects required with no loss in precision are becoming more necessary.

CONCLUSIONS

This double-blind study on afterpain reports data for 87 women given a total of 235 suppositories containing placebo, 5 mg., 10 mg., or 20 mg. dextromoramide. The results are tabulated and plotted to describe the most efficient techniques for comparing analgetic drug effects.

The calculations indicate that an analysis of all first doses administered gives a more precise dose response line than that obtained from patients given four balanced doses.

Additional arguments are presented to suggest that experimental plans using only first doses may in certain instances be more efficient in their use of the data collected, the facilities available, and their avoidance of practical complications which arise in medical research than plans using each subject as his own control.

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MEDICAL AND SURGICAL COMPLICATIONS ASSOCIATED WITH SEVERE POLIOMYELITIS

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THE patient severely disabled with poliomyelitis is predisposed to life-endangering complications which can occur in the acute or chronic stage of the disease. It is significant that these same complications occur with great frequency in other diseases, however the preferred methods of management are usually the same. The purpose of this paper is to report the experience of one respiratory and rehabilitation center with these complications and to illustrate how valuable experiences with severely involved poliomyelitis patients has resulted in better medical care for chronic disabilities of varied origin. The rehabilitation techniques and multidisciplinary approach can and has been applied to most areas in this medical center.

The diagnosis and management of severe poliomyelitis, with and without respiratory failure, has been discussed previously.[1]

PULMONARY COMPLICATIONS

Respiratory infections and atelectasis are common and serious complications occurring in patients with respiratory failure. Mild infections enhance the patient's respiratory demands by increasing metabolism while atelectasis and pneumonia also interfere with the alveolar exchange of respiratory gases. These complications may occur during the acute or convalescent period of the disease. Protective mechanisms are so diminished that such patients are susceptible to serious complications even with minor infections. When diminished ventilatory exchange is present, complications occur with surprisingly few clinical signs. During the acute phase loss of appetite, recrudescence of fever (with or without a polymorphonuclear leukocytosis), cyanosis, and disturbances in vital signs may be indicative of pulmonary infection or atelectasis. Serial tidal volume and vital capacity measurements provide a helpful index for early detection of these complications.

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Sudden reduction in tidal volume at high inspiratory pressure reflects a change in the mechanical properties of the lung and usually indicates the development of atelectasis. Roentgenographic changes, of course, are extremely important, but are usually observed after suspicion has been raised by other signs and symptoms. With intermittent positive pressure and/or the cuirass respirator a satisfactory chest roentgenogram can be obtained even in seriously ill patients requiring continuous artificial respiration. One cannot over emphasize the importance of periodic physical examinations of the chest in detecting complications in the early stage.

Prevention of respiratory complications should be constantly stressed to patients, visitors, and medical personnel. Those with suspected or obvious respiratory infections should not visit or come in close contact with these patients; also patients with early signs of respiratory infection should be isolated from the others. Culture of the nasopharynx, sputum, and tracheostoma if present, and drug susceptibility studies are valuable guides to therapy. In our experience as well as that of others[2] the use of prophylactic antibiotics is not warranted since a microbial flora of drug-resistant organisms such as *Pseudomonas aeruginosa* and *Bacterium proteus* may rapidly develop. The use of antimicrobial drugs should be reserved for vigorous treatment of established bacterial infections.

A number of factors favor the development of atelectasis in these patients. Probably the most significant in this respect is their inability to cough effectively, but concomitantly there exist diminished reflex protection of the airway, a propensity for aspiration, inadequate air exchange, and prolonged immobilization. The complexities of the cough mechanism and its various malfunctions created by poliomyelitis has recently been reviewed by Bosma.[3] With diminished ability to cough, bronchial aspiration may be reduced by judicious suction of secretions. One should not attempt to reduce secretion by the use of drugs since these result in thick tenacious mucus thereby increasing the possibility of atelectasis. Body position should of course be changed frequently. Humidification plays an important role in prevention and management of pulmonary complications. Mist helps to prevent drying and dessication of secretions in the tracheobronchial tree. For the tracheotomized patient using the tank respirator, one may use a small tube with a swivel fog outlet* through which humidified oxygen or air is delivered directly over the tracheostoma. This also serves as retractor for the tank collar permitting easier accessibility to the tracheostomy. Several other satisfactory types of humidification equipment are available, most being constructed on identical fundamental principles of nebulization. For the non-tracheotomized tank patient a special oxygen-box attachment developed at the Vanderbilt Poliomyelitis Respiratory and Rehabilitation Center has proved satisfactory (Fig. 1). It consists of a transparent plastic box enclosing the patient's head and attaching to the respirator. A high concentration of oxygen and humidity can be delivered through a nebulizer which is driven by oxygen under pressure. Temperature is thermostatically controlled. With some ingenuity, simple but practical modifications of this can be quickly assembled. For the

*Retracto-Tube with Mista-Fog Model 6P, Loewenstern Corp., Houston, Texas.

patient not in the tank respirator but requiring the cuirass or rocking bed, a portable humidifier may be very helpful.

The patient using the tank respirator most of the day should have periodic increases in intratank negative pressure several times daily in order to promote expansion and stretching of the chest musculature. Also by attaching the blower assembly of a vacuum cleaner to the porthole of the tank during expiration, positive pressure may be increased sufficiently to create a pressure gradient that causes a rapid expiratory air blast when the glottis is suddenly opened. This simulates a cough and helps the patient to clear his upper airway of excessive secretions. This procedure is beneficial only as a preventive measure and may be dangerous when atelectasis is present; it also requires voluntary synchronization of the patient's efforts and is of course ineffective when a tracheostomy is present. When glossopharyngeal breathing* has been mastered these procedures are not necessary since, as previously discussed,[1,4] this type of respiration is actually a form of intermittent positive pressure. The importance of this auxillary means of respiration cannot be overemphasized. In addition to increasing the vital capacity, it facilitates the simulation of an effective cough so vital in the prevention and treatment of respiratory complications. Specific breathing exercises should be given to all patients during periods of unassisted breathing.

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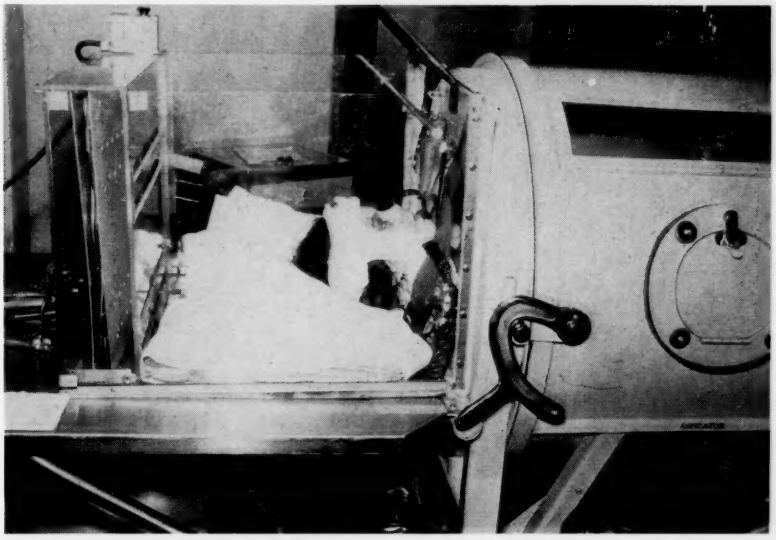

Fig. 1.—Oxygen-humidification apparatus for use with the tank respirator.

Except for glossopharyngeal breathing the most useful artificial coughing maneuver is achieved by mechanical exsufflation.† The lungs are expanded by

*Glossopharyngeal breathing, frequently referred to as "frog" breathing, is a maneuver whereby air in increments of approximately 50 ml. is forced into the tracheobronchial tree by the glossopharyngeal musculature. By a series of such "gulps" the patient can increase his "one-breath" vital capacity as much as three- or fourfold.

†Cof-flator, O.E.M. Corporation, East Norwalk, Conn.

positive pressure and then deflated by a sudden change to negative pressures of 20 to 30 mm. Hg. This causes a high expiratory flow rate introduced at the peak of inspiration. Secretions are "raised" by the expiratory blast (Fig. 2).

If collapse of large segments of one or more lobes occurs, bronchoscopy may be beneficial. This procedure when carried out early, judiciously, and, when necessary, repeatedly may be life-saving. Others describe good results with the use of Tryptar and other enzymes in the treatment of atelectasis.[5]

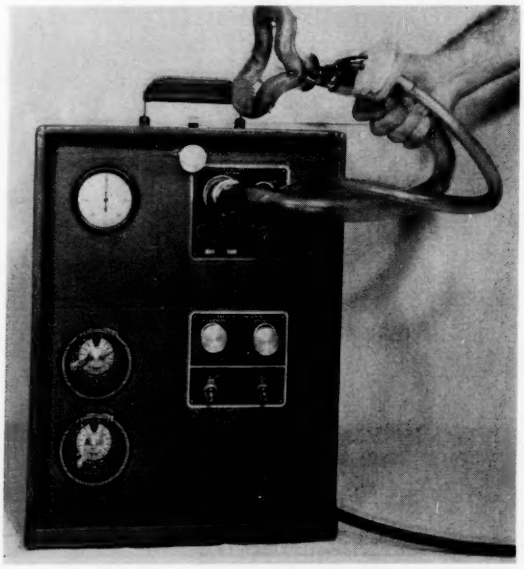

Fig. 2.—Cof-flator. A mouthpiece or a tracheostomy attachment may be used in place of the face mask.

URINARY TRACT

Although these complications may not be an early or sudden threat to life, as is the case with respiratory complications, they are nonetheless as important. As reduction in the mortality from acute poliomyelitis has occurred, the importance of urinary complications has become increasingly apparent. The ultimate objectives are only partially accomplished if the patient survives the acute illness only to develop renal insufficiency. This is probably the greatest problem in the long-term management of severe poliomyelitis. Our detailed experience with this is reviewed elsewhere.[6]

During acute poliomyelitis, especially in association with paresis of the lower extremeties and abdominal wall, urinary retention is not uncommon.[7] In one year, 38 of 169 patients with acute poliomyelitis had urinary retention.[8] Although it is usually temporary, we have observed several patients in whom urinary retention persisted for several weeks.

Patients should be urged to void frequently in order to avoid overdistention of the bladder and parasympathominetic drugs such as Prostigmin, Urecholine, and Furmethide are helpful. In our experience children respond better to Furmethide than do adults. This drug should be used with caution since it may provoke excessive respiratory secretions which are especially dangerous to the patient with respiratory insufficiency. It should be remembered that urinary tract infection is almost inevitable after bladder catheterization, and this procedure, especially indwelling catheterization, should be employed only as a last resort.[6] It has been shown that adequate urine specimens for culture in females can be obtained by using a "clean voided" technique.[6]

Urinary tract infection is extremely common in the extensively paralyzed patient. Fifty extensively paralyzed patients were studied over a 2-year period utilizing weekly cultures, urine examinations, and clinical evaluation; 44 had definite urinary tract infection, a large number being clinically severe and intractable.[6] Many had no symptoms referable to the urinary tract, and pyuria and leukocytosis proved to be unreliable clues to the presence of infection. The likelihood and severity of urinary tract infection were roughly proportional to the extent of paralysis, duration of immobilization, history of catheterization, and presence of urinary calculi. Urinary infection was more common in females, presumably due to greater chance for direct contamination of the urethra in women. All of these factors must be taken into account in the prevention and treatment of urological complications. Catheterization should be scrupulously avoided. Attention should also be directed to the effects of constipation and fecal impaction on bladder distention. The patient's position should be changed frequently, and during the postacute phase he should be instructed to lie in the prone position frequently, even when in the tank respirator. This facilitates drainage of the renal calyces. The "tilt table," wheel chair, and erect standing are also useful. Utilizing the clean voided technique[6] the urine should be cultured frequently and in vitro drug susceptibility tests should be performed. Gram-stained smears and bacterial counts of the urine are extremely helpful in distinguishing true urinary infection from contamination. The sporadic "positive" urine culture in the absence of significant bacteriuria does not require treatment. Prophylactic antimicrobial therapy is contraindicated since drug-sensitive pathogens are eliminated leaving resistant species not amenable to therapy. In general when antibacterial therapy is indicated, it should be intensive and for an adequate but not prolonged period. Combinations of antimicrobial agents may retard the development of drug-resistant stains.[9]

Urolithiasis is another major complication in the immobilized patient and is closely related to urinary infection as regards genesis and treatment.[6] Hypercalciuria secondary to bone demineralization, urinary infection, oliguria, and urinary stasis are factors that favor the development of urolithiasis. Most calculi in these patients are composed of calcium and phosphate oxalates and develop with surprising rapidity. The following measures are helpful in preventing and treating urolithiasis: (1) a diet not exceeding 0.5 Gm. of calcium daily should be instituted during the first 10 to 12 months of illness; (2) fluid intake of 3,000 ml. daily in adults and proportionate amounts in children should be employed;

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(3) excessive vitamin D intake should be avoided; (4) salicylates used prophylactically may increase the urinary solubility of calcium and thereby decrease stone formation to some extent; (5) in the treatment of ureteral colic, opiates should be used for relief of pain only if respiratory aids are available since the respiratory center can be depressed by these drugs; (6) renal irrigation with Suby's solution may be helpful in the dissolution of calculi but has not been extensively employed in these patients; (7) ureteral drainage and surgical removal of stones have a place in the management of these patients, but efforts should of course be directed against the fundamental etiologic factors.

Urologic complications are major obstacles in the total rehabilitation of severe poliomyelitis patients. These infections are usually insidius, asymptomatic, and chronic but unless eradicated will lead ultimately to renal insufficiency.

CARDIOVASCULAR COMPLICATIONS

Hypertension is common and may be hazardous in the severely involved poliomyelitis patient.[10] It is particularly prevalent in patients with bulbar or bulbospinal involvement and is probably neurogenic in origin. Stress created by respiratory aids or by anxiety undoubtedly plays a part, especially in the chronically involved patient. There is still no evidence that hypoxia contributes to hypertension, and our own evaluations lead us to the conclusion that the hypertension is not of renal origin. Transient elevation of the blood pressure frequently occurs during the acute phase and may indicate extension of the disease to the brain stem. Hypertension occurs in many of the more seriously disabled patients. These patients often experience headaches, confusion, convulsions, and occasionally cerebrovascular accidents. Antihypertensive drugs which will not inhibit the response to vasopressors should be employed, otherwise hypotension may ensue. The hydralazine derivatives and ganglionic blocking agents such as hexamethonium compounds are contraindicated for the above reasons in the management of acute hypertension. Reserpine in maximum dosage of 80 to 125 mcg. per kilogram of body weight per day is often helpful. Approximately one-fourth of the total dose is administered intramucularly or intravenously for rapid effect. This may be repeated every two hours if necessary. Magnesium sulfate, a vasodilator, may be helpful in controlling severe hypertension.

It is known that poliomyelitis causes myocarditis; however the frequency is usually not appreciated. Electrocardiographic and necropsy studies show that the incidence may be as high as 40 per cent during the acute illness. In our experience the clinical manifestations of myocarditis are inapparent or obscured by coexistence with other more overt manifestations of serious poliomyelitis. We have seen patients with confirmed poliomyelitis who died following cardiac arrhythmia secondary to myocarditis. One patient entered the hospital because of extreme tachycardia and fever. The examination was normal until 6 hours later when facial weakness occurred and spinal fluid findings suggested poliomyelitis. She developed fulminating bulbar manifestations and died without respiratory failure. Cardiovascular collapse is a common cause of death in acute poliomyelitis.[11,22]

Hypotension can occur as a manifestation of extensive brain stem involvement and should be prevented in order to preserve the vital functions of the central nervous system and kidneys. Continuous intravenous norepinephrine (4 mg. in 1,000 ml. of 5 or 10 per cent glucose) can be used to combat this problem.

Extreme hyperthermia is uncommon during the course of poliomyelitis but when present is indicative of involvement of the central temperature regulating mechanism. Cooling of the body should be attempted when temperatures are less than 104° F. Body temperatures in excess of 106° F. may occur and be associated with pale "clammy" skin. This apparently results from a lesion in the brain stem producing severe cutaneous vasoconstriction. One may assume that fever of this degree is of central origin, and measures should be used which will increase heat loss through cutaneous vasodilatation. Alternate applications of warm and cool sheets may be useful.

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Any patient immobilized for long periods of time may develop thrombophlebitis, and such is the case with severe poliomyelitis. These patients should be turned frequently and should receive passive exercise daily. The incidence of thrombophlebitis can be high,[12] but well-organized programs in physical therapy and good nursing care will do much toward reducing the complication. Once a thrombus has formed, every attempt should be made to prevent pulmonary embolism. Heat locally, elevation of the extremity, anticoagulant therapy, and venous ligation may be indicated.

With improvement in the survival rates of patients with serious poliomyelitis many new problems result from residual complications. Scoliosis is common and, if uncorrected, may lead to the development of severe cardiopulmonary disease. In most series of cases reported with kyphoscoliotic heart disease, poliomyelitis is a leading cause.

The clinical picture of kyphoscoliosis and heart disease is one of long-standing thoracic deformity frequently complicated by pulmonary infections or asthma, increasing exertional dyspnea, and finally congestive heart failure. This type of cardiopulmonary dysfunction may be manifest by clubbing of the fingers, cyanosis, anoxia, polycythemia, and carbon dioxide retention. There is apparently both compression and distention of the lungs resulting in abnormalities of alveolar diffusion of gases. Although there is not complete agreement,[37] most studies of this type of heart disease emphasize the relative short life expectancy. Chapman, Dill, and Graybiel,[38] in a comprehensive analysis of this problem, found that the life expectancy after the onset of severe cardiac failure or dyspnea was only five months. Case 1 is an example of this problem.

CASE 1.—P. J. C., a 10-year-old girl, had acute poliomyelitis at 18 months of age. She experienced respiratory difficulty over a 10-week period but never required respiratory aids. Following her acute illness there was progressive diminution in respiratory reserve and, despite spinal bone grafts, there was a further increase in kyphoscoliosis. She experienced frequent respiratory infections, "wheezing," and several bouts of bronchopneumonia. Two weeks before referral to Vanderbilt Hospital she developed an acute respiratory infection which was accompanied by cyanosis, dyspnea, and edema of the face, abdomen, and ankles. Oxygen had been given for 3 days prior to hospitalization. On admission she was orthopneic, cyanotic, and had severe kyphoscoliosis with extensive deformities of the thoracic cage. There was moderate intercostal weakness but the diaphragm moved well. Râles could be heard over both lung fields. The heart was en-

larged, and the pulmonic second sound was loud. There was hepatomegaly and ascites with presacral, periorbital, and dependent edema.

Her vital capacity was 100 ml. (normal for this age, approximately 1.63 liters), venous pressure 310 mm. saline, and the electocardiogram indicated a vertical position of the heart.

She was placed in the tank respirator and given oxygen, digitalis, and diuretics. Her course was progressively down-hill and she died 48 hours later.

Necropsy confirmed the clinical observations of cardiopulmonary failure secondary to the kyphoscoliosis.

NUTRITIONAL PROBLEMS

Nutrition does not present a significant problem in the management of the acutely ill patient except in the case of those patients with swallowing difficulty. In these instances nutrition may suffer temporarily but is not of importance when compared to the more serious complications of bulbar poliomyelitis. Other than the restriction of calcium-containing food to reduce calciuria, the nutritional considerations in acute poliomyelitis are insignificant. However, in chronic poliomyelitis, malnutrition is a major problem. Patients with extensive paralysis and immobilization have as much as 40 per cent loss of original muscle mass and body weight. This state of negative nitrogen balance continues for months. Recently we have had a new anabolic agent* under investigation which has promise in the management of the severely involved chronic poliomyelitis patient with extreme weight loss. If a dose of 1 mg. per kilogram per day is not exceeded, the drug is only slightly androgenic and promotes nitrogen retention. We have observed satisfactory weight gain in several patients treated with this agent.[14]

Excessive urinary excretion of calcium is inevitable during the first few weeks of illness.[13] Significant hypercalcemia leads to renal damage, impairment in cardiac conduction, and mental disturbances. This can be avoided by fluid intakes of 3,000 to 4,000 c.c. per day (in adults) which result in urinary dilution. Vitamin D supplements should not be added to the diet. It is traditionally felt that calcium must be restricted for months or years in these patients in order to reduce hypercalcemia and urolithiasis. There is preliminary evidence that calcium excretion reaches a negligible degree after several months and that it may be beneficial to supply normal calcium intake after this period. In this way severe osteoporosis of the vertebrae and other bones may be prevented.[15] Extensive bony demineralization makes spinal fusion procedures more difficult to perform and maintain.

METABOLIC DISTURBANCES

In poliomyelitis there are disturbances of water and electrolyte balance and alterations in the exchange of respiratory gases. During the acute phase of poliomyelitis the problem of water and electrolyte balance are in general similar to those of any acutely ill patient and will not be included in this discussion.

Alterations of oxygen uptake, CO_2 elimination, and serum pH adjustment are not uncommon in the seriously ill respirator patient and require the use of special laboratory aids in management. Hypoventilation with associated CO_2 retention

*Nilevar, Searle Laboratories.

may produce respiratory acidosis with lowered arterial blood pH. Conversely, hyperventilation with excessive CO_2 elimination may result in respiratory alkalosis with elevation of the arterial blood pH.[20,21] Mild hyperventilation (and respiratory alkalosis) is commonly seen in patients using respiratory aids, but this is fortunately well tolerated. Prolonged hyperventilation increases dependence upon respiratory aids as illustrated by Case 2.

CASE 2.—G. S., a 21-year-old white girl with respiratory failure, was transferred to the Respiratory Center 5 months following the onset of poliomyelitis. She had been the only poliomyelitis patient in a large general hospital and had special-duty nurses constantly. She had discovered that she was more comfortable at elevated respirator pressures and for several weeks had been using negative pressures up to 40 cm. of water in the cuirass respirator with high pressures in the tank respirator. On admission the arterial pH was 7.48, alveolar CO_2 22.8 mEq per liter and serum CO_2 content 16.4 mEq per liter, all evidence of chronic hyperventilation. With gradual reduction of pressure in the respiratory aids the laboratory values returned to normal. It was then possible to proceed with respiratory weaning, and on discharge from the center she was partially free of respiratory aids.

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A recently observed stress reaction occurring in patients with prolonged immobilization is associated with serious problems of fluid and electrolyte management.[23] Such patients are usually adolescents or young adults with marked loss of musculature. Frequently there is a history of fatigue from strenuous treatment programs or unrecognized respiratory insufficiency. The result is hypercalciuria, hypercalcemia, vague gastrointestinal disturbances, arterial hypertension, mental depression, irritability, fluid and electrolyte disturbances, labile water balance, and treatment-resistant hypokalemia. Renal function may be markedly impaired with reduced ability to concentrate urine and conserve body water. There is also evidence of adrenocortical alarm reaction with seborrhea, acne, hirsutism, and elevated urinary 17 ketosteroids. Case 3 is illustrative.

CASE 3.—W. B., a 30-year-old white man, was admitted to the Respiratory Center 9 months after the onset of poliomyelitis. He had quadriplegia and respiratory failure. He had spent most of these 9 months in the tank respirator but following admission displayed great enthusiasm in using the lesser respiratory aids and discontinuing the tank respirator. He made definite strides in his respiratory rehabilitation and was weaned entirely from the tank respirator; however, the vital capacity insidiously decreased, and he complained of fatigue. At this time he became somnolent; his general appearance became poor with pallor and extreme weakness. In addition he developed gastric distention, hypertension, and biochemical abnormalities. The serum potassium at this time was 2.3 mEq per liter and subsequently dropped to 1.7 mEq per liter despite parenteral supplementation of potassium. There was also hyposthenuria, slight elevation of nonprotein nitrogen, hypernatremia, and polyuria. The serum calcium rose to 13 mg. per 100 ml. The patient was immediately placed in the tank respirator and the rehabilitation program temporarily discontinued. Gradual improvement in both the clinical and electrolyte abnormalities occurred. In retrospect, respiratory weaning had been allowed to proceed too rapidly, and the patient had been placed under stress that he could not tolerate.

This syndrome in most instances may be abolished by retrenching the rehabilitation program and supplying maximum respiratory assistance.

GASTROINTESTINAL COMPLICATIONS

These complications are frequent in the seriously ill poliomyelitis patient, and particularly those with medullary center and/or bulbar involvement. Specific

gastrointestinal lesions may result from hypothalamic involvement.[24] During the acute illness the lesions of the intestinal tract consist primarily of petechiae, ulcerations, and hemorrhage. The patient complains of mild abdominal pain or abdominal distention and may refuse food because of the resultant discomfort. Frank bleeding occurs infrequently but may be massive. Many patients with bulbar involvement have occult blood in the stool with no clinical manifestations of intestinal hemorrhage. Gastrointestinal bleeding is not uncommon in the chronic stage of poliomyelitis. Hemorrhage is usually accompanied by abdominal distention, and massive bleeding may be an immediate cause of death. The treatment of gastrointestinal ulceration and bleeding is similar to that of the non-poliomyelitis patient with a similar complication.

Gastrointestinal distention is common during the acute and convalescent phase and is augmented by failure to coordinate with respiratory aids and psychological factors. This limits respiration further by elevating the diaphragm. Prompt aspiration of stomach contents is indicated and may be life-saving in that it relieves distention and prevents aspiration of vomitus.

Constipation and fecal impactions, though not dangerous, constitute an annoying and common problem in these patients and are particularly prone to develop in immobilized patients with extensive paralysis. If necessary, fecal impactions should be manually removed. A word of caution should be given concerning the use of repeated tap water enemas; this can result in significant loss of sodium and in some cases also of potassium.[25] A program of daily bowel elimination should be initiated for each patient. There is no laxative which is universally effective. Mineral oil should be avoided because of the danger of aspiration and lipid pneumonia.

DECREASED PULMONARY COMPLIANCE

The elasticity and flexibility of the lungs and thoracic wall is often decreased in the patient with respiratory impairment due to poliomyelitis.[26] This increases the work of breathing, diminishes the efficiency of mechanical respiratory aids, and makes weaning more difficult. For clinical purposes decreased compliance can be estimated by measuring serial tidal volumes with a spirometer at various pressure gradients while the patient is in the tank respirator. This problem is illustrated by Cases 4 and 5 and the observations in Fig. 3.

CASE 4.—S. B., a 27-year-old man, was admitted to the Poliomyelitis Respiratory Center during the acute stage of poliomyelitis. He rapidly developed respiratory failure, his vital capacity dropping to a low of 350 ml. After the acute stage, methods to increase his chest expansion including specific breathing exericses, intermittent positive pressure breathing, periodically increasing the respirator pressures, and training in glossopharyngeal breathing were initiated and maintained. He attained complete unassisted breathing in 5.5 months.

CASE 5.—On the other hand, W. B., a 30-year-old man, was admitted 9 months after the onset of poliomyelitis with respiratory failure. He had been confined to a hospital where he had spent virtually twenty-four hours daily in the tank respirator with no specific measures to preserve pulmonary compliance. His vital capacity remained between 500 and 550 ml., and very little success in weaning was achieved until methods to counteract the decreasing pulmonary compliance were instituted. His vital capacity progressively rose to a maximum of 1,000 c.c., and as a result of this it was possible to wean him to lesser respiratory aids.

As noted in Fig. 3 the lung volume change of W. B. remained comparatively resistant to increasing respirator pressures whereas that of S. B. increased considerably more under the same conditions. The slight increase in tidal air in W. B. with greater respirator pressures indicates decreased elasticity or compliance of the thoracic wall and lungs.

Immediately after the acute illness, measures should be taken to preserve pulmonary compliance. Specific breathing exercises, intermittent positive pressure breathing, increasing respirator pressures for short periods daily, artificial coughing maneuvers, and glossopharyngeal breathing are all important in this respect.

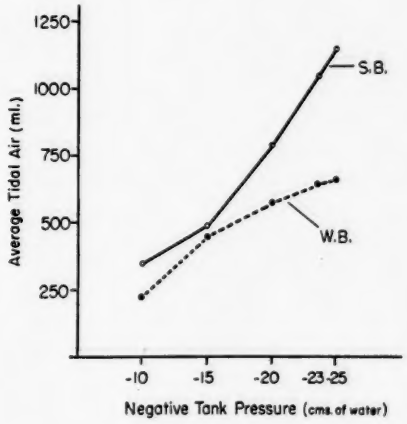

Fig. 3.—Changes in pulmonary compliance in two patients.

PSYCHIATRIC AND SOCIOECONOMIC COMPLICATIONS

Seidenfeld[27] has emphasized the emotional impact of severe poliomyelitis on patients and their families and Prugh and Tagiuri[28] have outlined the psychiatric problems of the respirator patient. There is probably no other disease for which the public has so much fear and anxiety. Many factors contribute to this—the contagious aspects of the disease causing concern for other members of the family and community, individuals developing guilt feelings regarding failure to observe publicized precautions against the disease, and widespread fear of the crippling aspects of poliomyelitis. Most patients with severe poliomyelitis are anxious and apprehensive from the onset. Later in the postacute and convalescent phase there is shocklike awareness of the severity of the illness, associated with negativism, dependency, and emotional lability. This is usually associated with or followed by denial of disability and with guilt reactions which lead to resentment or open hostility to the medical staff or family. Long-term hospitalization causes tremendous anxiety in relation to financial aspects, separation from family, marital relationships, and parental responsibilities.

Detailed discussion of management of these complex problems is beyond the scope of this paper. The members of the medical staff should recognize those individuals whose personality structure is not sound enough to withstand the natural reactions to such a catastrophic illness. They should be alert to the excessive or protracted responses and inappropriate social behavior which indicate inability to cope with such physical handicaps. This group of patients and their families should receive the support of the entire staff and more than perfunctory assistance in coping with this illness. Psychiatric aid is indicated for the severely involved patient before serious problems develop. The psychiatrist should assist in the coordination of the objectives of the medical team.

The socioeconomic aspects of serious poliomyelitis are enormous. This is especially true if the breadwinner of the family is involved with severe crippling. The average length of hospitalization for each of 80 respirator patients prior to their transfer to this Center was 268 days. The average cost per patient was approximately $3,037.[4] It is obvious that few families can meet this expense. However, this is only a fraction of the problem since economic burdens continue when the patient is discharged to home care. The effort required in such a rehabilitation venture is obvious. It requires the aid and cooperation of internists or pediatricians, vocational counselors, psychiatrists, social workers, and charitable organizations, especially the National Foundation for Infantile Paralysis. The complete revamping of physical environment and mental attitude of an entire family unit is an enormous task that may involve an entire community and extend over a period of years.

ANESTHESIA AND SURGERY IN RESPIRATOR PATIENTS

In the past it was felt that surgical procedures necessitating anesthesia to respirator patients was virtually impossible. However, with the coordination and utilization of important advances in anesthesia, surgery, and respiratory physiology, major thoracic and abdominal surgery can be carried out successfully. Poliomyelitis complications that may lead to anesthesia and surgery include urological procedures (cystoscopy, nephrolithotomy, nephrectomy, and others), pregnancy (vaginal delivery, Caesarean section), orthopedic reconstruction, and tracheostomy management. Acute surgical problems can of course arise in any patient at any time and are more common in the already debilitated patient.

The details of the conduct of anesthesia and surgery have been outlined.[19,29,30] Only a few important principles will be mentioned. Preoperative preparation is unique and includes emotional acceptance by the patient, minimal premedication, fluid and blood supplements, and the anticipation of a poor vasomotor adjustment. In patients undergoing extensive procedures, inhalation agents (especially cyclopropane) with endotracheal intubation and assisted or controlled respiration are usually prescribed. Intravenous barbiturates are contraindicated because of possible respiratory depression. Anesthesiologists do not in general condone spinal anesthesia for paralytic cases although it would seem to be the anesthesia of choice. This is more due to the psychic effect on the patient rather

than for a physiological reason. Following endotracheal intubation a tracheostomy may be necessary to preserve a patent airway. Muscle relaxants are rarely necessary especially for the extensively paralyzed patient. Regional anesthesia may be indicated for specific procedures such as reconstructive hand surgery; however, brachial blocks should be performed only under expert guidance because of the possibility of pneumothorax in a patient who has pre-existing pulmonary insufficiency.

A distinct advance in anesthesia occurred with the development of the Jefferson ventilator* which automatically provides a predetermined tidal air exchange during anesthesia.

Postoperatively, the tank respirator is usually indicated since the cuirass or rocking bed may be uncomfortable following thoracic or abdominal procedures and since maximum ventilation is best achieved by this means.

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PREGNANCY COMPLICATING POLIOMYELITIS

Pregnancy increases susceptibility to severe manifestations of acute poliomyelitis.[16a,b] Poliomyelitis tends to be more severe as pregnancy progresses and fetal mortality is increased.[17] Spontaneous abortions may occur early and in the mid-portions of pregnancy, and premature labor is not uncommon. Maternal death is usually a result of severe paralytic disease or the failure of physicians to detect insidious respiratory insufficiency caused by a combination of poliomyelitis and pregnancy.[18] A few principles in the management of these patients can be listed.[17,19]

1. The complications of pregnancy are treated in the same manner as pregnancy in the nonpoliomyelitis patient.

2. The course of the disease usually does not modify obstetrical care.

3. Caesarean section is not indicated except for obstetrical reasons. Acute bulbospinal involvement with severe respiratory insufficiency occurring late in pregnancy may be an exception, and toxemia or intractable urinary infection may necessitate induction of labor in the last month of pregnancy.

4. Routine care: (a) Frequent changes in body position, stretching of the hip musculature. (b) In the latter stages of pregnancy, the combination of pregnancy and respiratory muscle paralysis often produces progressive pulmonary insufficiency; therefore pressure increases in the respirator may be necessary for adequate ventilation. The patient should become accustomed to the dome attachment to the respirator or to intermittent positive pressure breathing devices necessary for obstetrical examination, nursing care, and delivery. The chest and rocking bed are usually contraindicated in late pregnancy because of discomfort and inadequate ventilatory function. (c) Reassurance of the mother throughout concerning the expected normal outcome is imperative.

5. Spontaneous labor may proceed rapidly when the expulsive force of the uterus is unopposed by voluntary skeletal musculature. Pudendal blocks may be employed and delivery carried out on the carriage of the respirator by employing intermittent positive pressure breathing through a mask or by a respirator dome.

*Air-Shields, Inc., Hatboro, Pa.

6. The newborn infant should be isolated for approximately two weeks.

TRANSPORTATION

Problems associated with the transportation of patients with respiratory impairment have been outlined in previous papers by Hunley,[31] Brahdy,[32] and Wilson.[33] This is a tremendous task which requires the coordination and cooperation of many agencies and individuals. We have found a portable tank respirator* extremely helpful in both air and train transportation of respirator patients. As a general rule transportation can best be arranged through contact with the National Foundation for Infantile Paralysis.

Fig. 4.—Resting position of a patient with severe orthodontic and maxillofacial deformities following poliomyelitis.

OTHER COMPLICATIONS

It has been shown that directly or indirectly severe poliomyelitis produces a hearing loss which follows a consistent pattern, and it is greater in the more severely disabled patients. There is a mild but significant impairment of hearing for both pure tones and speech, and for both bone- and air-conducted stimuli. Preliminary data suggest a neurogenic defect produced possibly by the poliomyelitis virus or by hypoxia.[34]

*Port-a-Lung, J. J. Monaghan Co., Denver, Colo.

Orthopedic deformities are of utmost importance in these patients, but because of technical aspects are beyond the scope of this discussion. Good physical therapy programs early in the course of the disease will prevent many of these complications. Surgical correction of deformities at the appropriate time and in selected patients is essential in the total care of these patients.[35] This has been adequately discussed.[36] Severe orthodontic problems may arise as a result of extensive paralysis of cervical and facial musculature (Fig. 4).

SUMMARY

With newly acquired knowledge, advances in technology, more suitable medical equipment, and broader application of the multidisciplinary approach to total rehabilitation, the complications in severe acute illnesses and chronic disability can be controlled in a much better fashion than previously.

The detection and treatment of these complications are usually the same whether they occur in patients with poliomyelitis or in patients with other diseases. It is important that we do not cast aside lessons learned in the management of severe poliomyelitis. We should apply these same methods and techniques to other chronic disabilities, which will certainly increase in number as physicians become more and more proficient in the management of acute illnesses.

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OBSERVATIONS ON POSSIBLE FACTORS RESPONSIBLE FOR THE SEX AND RACE TRENDS IN CARDIOVASCULAR-RENAL MORTALITY IN THE UNITED STATES

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INTRODUCTION

DURING the years 1947-1950, an extensive effort was made in the Public Health Service to bring together and analyze statistics on morbidity and mortality in the general population due to cardiovascular-renal (C-V-R) diseases. A series of nine papers was published, seven dealing with mortality statistics and two with morbidity statistics from the National Health Survey of 1935-1936.[1-9]

In the last of this series of reports,[9] particular attention was called to several phenomena (Fig. 1).

1. ". . . the increasing risk of death from the major cardiovascular-renal diseases among white males between the ages 35 and 64 years . . ."

2. ". . . an upward trend in the death rate for these diseases among white males while the corresponding rates for white females are going down. . ."

3. "In 1920, the difference between the two sexes was negligible while in 1947 the white male rate exceeded that for white females by 100 percent at 35-44 years of age, 120 percent at 45-54 years of age, and 97 percent at 55-64 years of age."

4. ". . . the marked excess in nonwhite mortality in (these) age group(s) . . ."

5. ". . . the sex differences in the trends of nonwhite cardiovascular-renal mortality in these same ages are trivial."

6. "In the white population, the contrast between the sexes is very much greater for the circulatory and kidney diseases than it is for the other causes of death. . . The death rate among white males in the working ages is not increasing for all other causes of death combined."

After the completion of the heart disease statistical studies, it seemed worth while to ascertain the views of experts regarding these particular findings. Accordingly, in February, 1952, a letter of inquiry, together with a reprint of the

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final paper of the heart disease series, was sent to 47 individuals, 26 of whom replied.

The objectives of the present report are to: (1) bring the cardiovascular-renal mortality statistics up to date through 1955; (2) present additional statistics on age-sex-race-group death rates for *specific* cardiovascular-renal diseases, e.g., arteriosclerotic heart disease, hypertensive cardiovascular disease, etc., and re-examine the problems previously posed in the light of these data; (3) summarize the replies of the expert consultants to the inquiry; and (4) note recent relevant research findings.

CARDIOVASCULAR-RENAL MORTALITY STATISTICS, U. S., 1920-1955

Since the publication of the original study on race and sex differentials in cardiovascular-renal mortality trends, data have accumulated for 8 additional calendar years (Fig. 1).* The additional data generally indicate a continuation of the trends previously observed for the period 1920-1947. Thus, the gap in cardiovascular-renal death rates between middle-aged white men and white women has widened further. This is due principally to the continued gross decline in the death rates for white females. The rates for white males in the age groups 25 to 34, 35 to 44, 45 to 64 rose fairly steadily during the 20 to 25 years following 1920, were relatively constant from the early 1940's to the early 1950's, and seemed to be declining slightly in the mid-1950's. Only in the age group 25 to 34 was there a general downward trend in the death rate for adult white males over the entire period 1920-1955. Here, the rate for white females was declining more markedly.

Throughout the 35-year period, rates for the nonwhites were consistently higher than those for the whites. This differential remained, despite the tendency in the death rates for nonwhites to decline. This fall, more marked in the younger than in the older age groups, was under no circumstance as great as the reduction in cardiovascular-renal mortality rates for white females.

In contrast to the whites, the nonwhites exhibited no gross tendency over these decades to develop a sex differential in mortality rates. However, there may now be a slight indication of change in this direction. Thus, the nonwhite female rates were uniformly higher than the nonwhite male rates in the 1920's, whereas by the 1950's they were consistently (but only slightly) lower.

STATISTICS ON MAJOR COMPONENTS OF THE CARDIOVASCULAR-RENAL DISEASE MORTALITY, UNITED STATES, 1955

The category, *cardiovascular-renal (C-V-R) diseases*, is a broad, heterogeneous grouping. It includes several specific disease entities of different etiologies, e.g., arteriosclerotic heart disease (ASHD) including diseases of the coronary arteries, hypertensive cardiovascular disease, cerebrovascular diseases, rheumatic heart disease, etc.

*These rates were computed on a slightly different basis from the rates published in the previous report.[10] Also, the Sixth Revision in the International Statistical Classification of Diseases and Causes of Deaths (I.S.C.) which went into effect in 1949, produced a relatively minor discontinuity in cardiovascular-renal mortality trends.[11] Neither of these factors will alter the conclusions.

In order to arrive at a more precise estimate of the meaning of the cardiovascular-renal mortality trends for the period, 1920-1955, an examination of the specific components of the cardiovascular-renal grouping is needed. However, changes in medical concepts, diagnostic skills, disease classification, and certification practices over the past 35 years make it virtually impossible to reconstruct valid trend lines for the various components of the cardiovascular-renal disease grouping. Therefore, it is very difficult to determine definitively the precise basis for the divergence in mortality trends between white men and women and the basis for the persistent differential in rates between whites and nonwhites. However, it is possible to clarify these problems by examining data for a recent year.

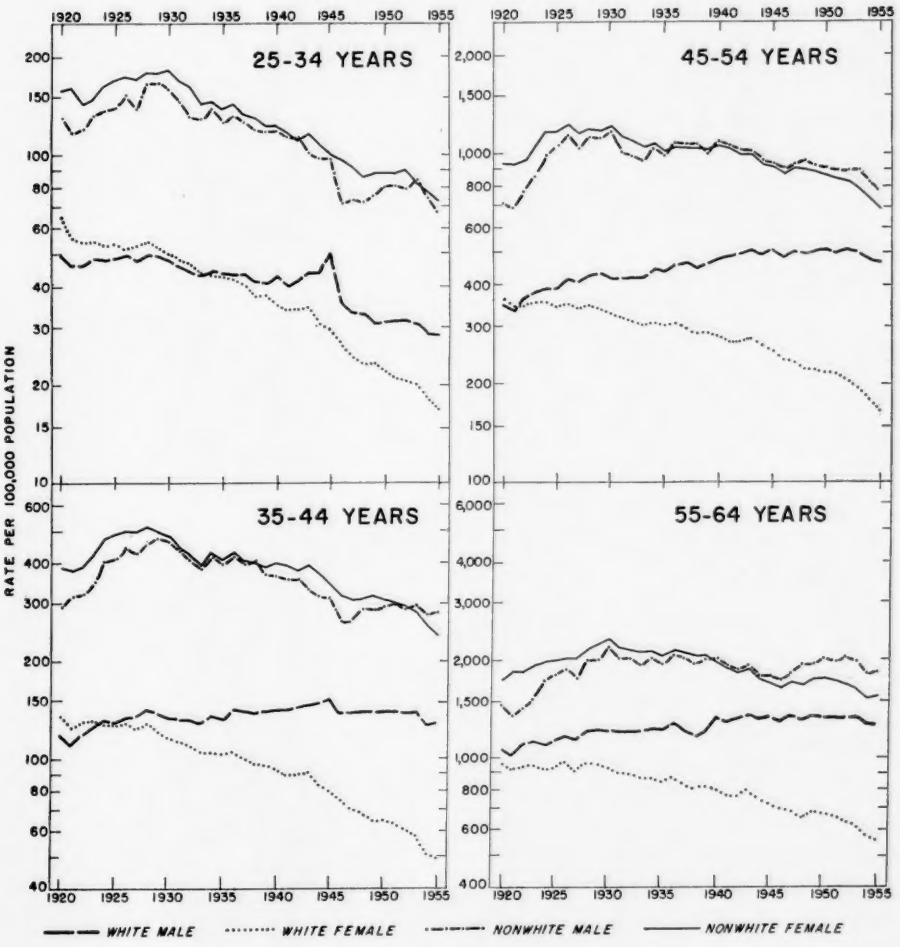

Fig. 1.—Death rates for major cardiovascular-renal diseases by race and sex for age group 25 to 64 years: United States, 1920-1955.

TABLE I. DEATH RATES AND RATIOS FOR SELECTED CAUSES BY COLOR, SEX, AND SPECIFIED AGES: UNITED STATES, 1955

CAUSE OF DEATH	RATES															
	WHITE								NONWHITE							
	MALE				FEMALE				MALE				FEMALE			
	25-34 YEARS	35-44 YEARS	45-54 YEARS	55-64 YEARS	25-34 YEARS	35-44 YEARS	45-54 YEARS	55-64 YEARS	25-34 YEARS	35-44 YEARS	45-54 YEARS	55-64 YEARS	25-34 YEARS	35-44 YEARS	45-54 YEARS	55-64 YEARS
All Causes	168.1	338.1	909.5	2190.2	87.9	197.7	461.7	1118.5	401.9	758.1	1571.0	3196.7	276.6	583.6	1262.2	2425.0
Major cardiovascular-renal diseases 330-334, 400-468, 592-594	29.0	129.4	467.7	1263.5	16.8	48.9	164.3	550.8	66.9	282.0	775.5	1825.9	71.9	240.0	682.7	1540.0
Vascular lesions affecting central nervous system 330-334	4.2	11.6	45.2	157.5	3.5	11.5	40.2	119.8	13.2	60.1	161.5	451.7	15.2	62.9	200.1	463.4
Arteriosclerotic heart disease, including coronary disease 420	10.8	82.9	328.7	856.3	1.9	12.6	60.7	263.8	14.8	82.2	279.9	653.0	12.4	44.9	169.5	413.0
Other myocardial degeneration 422	0.6	2.8	11.3	40.8	0.4	1.5	5.9	23.9	4.2	14.3	40.3	114.4	3.9	11.0	40.2	93.0
Hypertension 440-447	1.3	6.0	24.1	82.6	0.7	4.5	18.7	68.7	14.0	67.2	170.2	359.2	14.2	67.5	169.7	371.3
All other 400-419, 421, 423-439, 448-468, 592-594	12.2	26.0	58.5	126.3	10.3	18.8	38.8	74.7	20.7	58.2	123.5	247.6	26.1	53.7	103.2	199.3

CAUSE OF DEATH	RATIOS*															
	WHITE MALE TO NONWHITE MALE				WHITE FEMALE TO NONWHITE FEMALE				WHITE MALE TO WHITE FEMALE				NONWHITE MALE TO NONWHITE FEMALE			
	25-34 YEARS	35-44 YEARS	45-54 YEARS	55-64 YEARS	25-34 YEARS	35-44 YEARS	45-54 YEARS	55-64 YEARS	25-34 YEARS	35-44 YEARS	45-54 YEARS	55-64 YEARS	25-34 YEARS	35-44 YEARS	45-54 YEARS	55-64 YEARS
All Causes	.42	.45	.58	.69	.32	.34	.37	.46	1.91	1.71	1.97	1.96	1.45	1.30	1.24	1.32
Major cardiovascular-renal diseases 330-334, 400-468, 592-594	.43	.46	.60	.69	.23	.20	.24	.36	1.73	2.65	2.85	2.29	.93	1.18	1.14	1.19
Vascular lesions affecting central nervous system 330-334	.32	.19	.28	.35	.23	.18	.20	.26	1.20	1.01	1.12	1.31	.87	.96	.81	.97
Arteriosclerotic heart disease, including coronary disease 420	.73	1.01	1.17	1.31	.15	.28	.36	.64	5.68	6.58	5.42	3.25	1.19	1.83	1.65	1.58
Other myocardial degeneration 422	.14	.20	.28	.36	.10	.14	.15	.26	1.50	1.87	1.92	1.71	1.08	1.30	1.00	1.23
Hypertension 440-447	.09	.09	.14	.23	.05	.07	.11	.19	1.86	1.33	1.29	1.20	.99	1.00	1.00	.97
All other 400-419, 421, 423-439, 448-468, 592-594	.59	.45	.47	.51	.39	.35	.38	.37	1.18	1.38	1.51	1.69	.79	1.08	1.20	1.24

From the Department of Health, Education and Welfare, Public Health Service, National Office of Vital Statistics, Washington 25, D. C.

Includes only deaths occurring within the continental United States. Rates per 100,000 estimated mid-year population in each group residing in area. Numbers after causes of death are category numbers of the Sixth Revision of the International Lists, 1948.

*Ratios computed from rates per 100,000 population.

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The 1955 data indicate that a very large part of the differential in the cardiovascular-renal death rates for middle-aged white women and white men can be ascribed to the higher mortality from arteriosclerotic heart disease among the men (Table I). From 83 to 88 per cent of the sex differential in the C-V-R death rates among whites was accounted for by the higher ASHD death rates among men in the age groups from 35 to 64 years. These relationships are illustrated graphically for a single 10-year age group in Fig. 2.

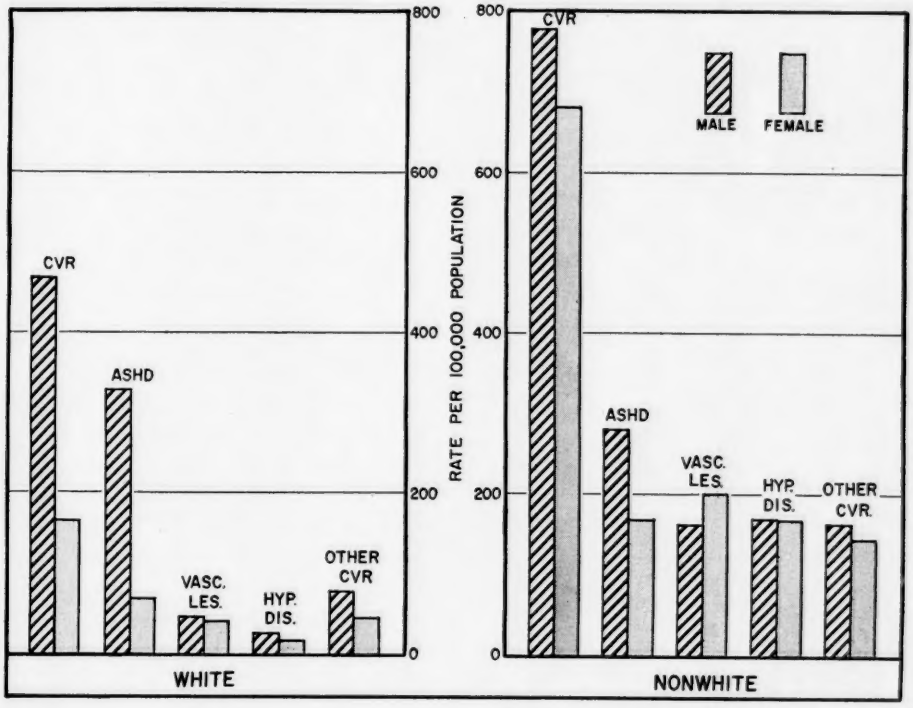

Fig. 2.—Death rate for specified components of major cardiovascular-renal diseases by race and sex for age group 45 to 54 years: United States, 1955.

The basis for the higher C-V-R death rates for nonwhites as compared with those for whites is also clarified by the analysis of the component parts (Table I and Fig. 2). Among men, the higher C-V-R death rates in the age groups 35 to 64 years are brought about by the higher mortality rates among the nonwhites for hypertensive disease and its sequela, cerebrovascular disease.* With respect

*The I.S.C. grouping, *Vascular Lesions Affecting the Central Nervous System* (330-334), is a composite category structured on a pathologic—rather than etiologic—basis. It includes deaths from embolism, thrombosis, and hemorrhage, and embraces several specific etiologic processes. Further, the rules for coding deaths to a single underlying cause provide that certificates listing both cerebrovascular and hypertensive disease be classified to cerebral vascular lesions. Considerable evidence is available indicating that hypertensive disease is actually the basic etiologic process in a majority of cerebrovascular deaths in middle-aged persons.[12-14] It is for this reason that the sex race patterns for cerebrovascular disease death rates on middle age are similar to those for hypertensive disease; both are far higher in nonwhites than whites (Table I).

to the race differential in the death rates for the females, the rates are substantially higher for the nonwhites for every major component of the cardiovascular-renal diseases.

The sex difference in cardiovascular-renal mortality among nonwhites is relatively small as compared with the marked differential existing among the whites. Just as for the white population, the largest sex difference among nonwhites is in the death rates for arteriosclerotic heart disease. Here, however, the sex ratio ranges only from 1.2 to 1.8 as contrasted with 3.2 to 6.5 for the whites —a phenomenon attributable to the relatively high ASHD death rates in nonwhite women compared with white women (Table I). The other major C-V-R components do not exhibit any great excess of mortality among nonwhite men as compared with nonwhite women. In fact, the opposite is frequently the case; hence the smaller sex differential, compared with that for the whites.

The largest contributor to the sex difference in cardiovascular-renal mortality in 1955 is found to be arteriosclerotic heart disease. The question, therefore, arises whether ASHD was decisively responsible for the divergence in the male-female cardiovascular-renal mortality trends for adult white persons from 1920 to 1955.

With respect to this problem, it is readily possible to conclude that these trends *cannot* be attributed to certain of the other etiologic entities in the heart disease group, e.g., rheumatic heart disease. For all sex-race groups, the infectious diseases declined as causes of death over the period 1920-1955. The fall in mortality from these diseases for both sexes must certainly have been accompanied by corresponding changes in one etiologic subgroup of the C-V-R total—the C-V-R infectious diseases. In fact, the decrease in mortality rates for infectious diseases, together with the decline in deaths from cardiovascular-renal complications and sequelae of pregnancy and the puerperium, was almost certainly a significant factor in the over-all lowering of the C-V-R death rates among whiet women. The death rates for white men were undoubtedly affected by the declining rate for infectious diseases, but probably not to the same extent as those for women. However, increases in total C-V-R mortality for white men are observed which indicate that other factors had more than counterbalanced the effect of the decline in infectious diseases. This seems to rule out the C-V-R infectious disease component as a major factor in the divergency in trend between the sexes.

What can be said regarding the role of hypertensive disease, another major etiologic category in the C-V-R group? The possibility that hypertensive disease played a part cannot be definitely assessed on the basis of available data. The difficulty of evaluating trends of mortality from hypertension is not only a product of evolving patterns of diagnosis and classification over the 35 years; it is further complicated by the present rules for coding, which provide that hypertensives dying of myocardial infarction or other forms of coronary disease be coded to ASHD (category 420 in the International Statistical Classification). Hence, it is almost impossible to arrive at an accurate estimate of the totality of hypertensive deaths, or to distinguish between hypertensive and nonhypertensive cases of arteriosclerotic heart disease. This is particularly important for the problem of ASHD mortality trends in nonwhites compared to whites.[16]

To add to the complexity of the problem, there is a possibility that changes in medical concepts, diagnostic skills, and certification practices may have influenced physicians to certify ASHD more frequently as a cause of death.[15] However, of all these possible artifacts in the hypertensive disease and ASHD mortality statistics there is one thing that can be said. If they exist, there is no evidence available to suggest that they would operate with a sex bias, effecting a rise in white male and a decline in white female C-V-R death rates. In fact, if these artifacts have been the decisive factors accounting for the recorded white male trend, there is left the even greater difficulty of explaining why they have not affected the white female mortality in a similar manner.

All in all, it seems most likely that the largest part of the divergence in trend for the two sexes in cardiovascular-renal mortality among white middle-aged persons results from a sizable, real increment in the male death rates for arteriosclerotic heart disease, a disease known to cause higher mortality among men.* The emergence of arteriosclerotic heart disease as an even more important problem, absolutely and relatively, particularly in the susceptible sex, would, in combination with the downward trends for certain other disease, amply account for the observed patterns of evolution of C-V-R mortality in middle-aged white persons from 1920 to 1955.

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OPINIONS OF EXPERT CONSULTANTS CONCERNING THE 1920-1947 CARDIOVASCULAR-RENAL MORTALITY TRENDS

After completion of the original heart disease statistical studies,[1-9] a query was undertaken to ascertain the views of experts concerning the findings. A letter of inquiry was prepared and dispatched, together with a reprint of the final paper of the heart disease series.[9] After giving some of the background and the findings of the study, the letter asked the experts to give their answers to specific questions.

"1. What medical, social, or environmental changes have taken place in the past 25 years which in your opinion could account for an increase in cardiovascular-renal mortality among white males in the working ages at the same time that mortality from these causes among white females was declining?

"2. What experiments, research, or statistics can you suggest that you believe would throw further light upon this divergence in the male and female mortality?"

No claim is made that the replies constitute a representative sampling of expert opinion. The chief purpose of the inquiry was to obtain suggestions of hypotheses for future testing. The opinions expressed were abstracted in as

*This is not consistent with the conclusions of another recent study, viz. ". . . the real increase in mortality from this disease has been relatively small . . .."[15] This analysis, involving data for a 15-year period, 1940-1955, dealt with a composite index, the age-adjusted death rate. These age-adjusted rates, weighted heavily by the preponderant number of deaths in the older age groups, tend to obscure the trends during middle age. Further, in presenting C-V-R mortality trends, this report made no distinction with respect to sex and race. The importance of these methodological differences is illustrated by the fact that the data as analyzed indicated a decline in C-V-R mortality rates from 1940 to 1955, a finding used to support the conclusion that a large part of the observed rise in coronary disease rates is artificial. It is clear, however, that when an analysis of the trends by age, sex, and race is made, the results, particularly for white men, are quite different.

objective a manner as possible to summarize the views. Of the 47 individuals queried, 26 replied; 7 were public health statisticians, 4 sociologists, 2 gerontologists, and 13 cardiovascular disease specialists. The replies frequently went beyond the two questions that had been posed and dealt with the following problems.

Were the Delineated Statistics Valid? This problem was posed by both statisticians and physicians. Considered over-all, the answer was in the affirmative, with qualifications. It was emphasized that changes in diagnosis, terminology, classification, and reporting might have exerted a sizable influence on the statistical trends. These effects were practically incapable of precise quantification. They became a major problem particularly with any attempt to focus on changes over the decades in incidence of specific diseases, e. g., coronary disease[15-24] (see foregoing and subsequent discussion). Despite these difficulties, it was generally agreed that the reported trends were valid qualitatively. Further, with the definitive decline in infectious disease death rates (both C-V-R and non-C-V-R infectious diseases) among all 4 sex-race groups, it was necessary, in order to account for the observed trends, to identify a disease process coming to the fore, relatively and absolutely, which had a clear-cut predilection for males. Long-standing, conclusive evidence was referred to demonstrating that coronary disease occurred with manifold greater frequency in middle-aged men than women.[21,24] Prominent cardiologists drew upon the experience of their long careers to infer that the increase in diagnosed cases of myocardial infarction could not be accounted for simply by enhanced diagnostic acumen. It was their conviction that this disease had in fact sizably increased in incidence among middle-aged men since 1920.

What Factors Were Responsible for the Increase in Cardiovascular-renal Mortality Rates in White Males From 1920 to 1947? As already indicated, practically all respondents with a medical background implicated coronary disease (arteriosclerotic heart disease) as the specific entity which had increased in incidence and was therefore responsible for the observed white male mortality trend, and, in view of the white female insusceptibility, the emerging sex differential.* The discussion therefore focused on etiologic factors possibly responsible for this increase in coronary disease in middle-aged men.

The replies indicated wide areas of agreement in thinking, irrespective of scientific background and discipline. Thus, it was recognized that purely endogenous, inherited factors almost certainly could not by themselves account for the observed trend, for 27 years is far too short a time to bring about basic changes in inherent human biology. Thus, the increase in male C-V-R death rates and the emergence of a sex differential could hardly be due simply and exclusively to an endogenous alteration, developing in one generation, in coronary artery anatomy, in lipid metabolism, or in sex endocrinology. There might be long-standing innate differences between the sexes along these lines. But these could play a role in producing the relatively rapid emergence of a gross sex differential only in interaction with relatively new (qualitative and/or quantitative) exogenous, environmental factors.

*A few respondents also placed emphasis on hypertension, as such, and in relationship to coronary disease.

Although stated in a brief fragmentary fashion by only a few respondents, this inference was apparently implicit in the replies of virtually all, for each one focused on environmental, sociologic factors possibly accounting for the white male increase in cardiovascular-renal and coronary disease mortality.

Among these possible factors, considerable attention was given to diet. It was suggested that in recent decades men in the United States had increased their consumption of fats, particularly animal fats (meat, butter, eggs, etc.). It was further indicated that obesity may have become more common, due to increasing imbalance between caloric intake and energy expenditure, with the former remaining high or becoming higher, and the latter declining as work became less arduous. It was suggested that these changes in pattern of diet and incidence of obesity may be influencing cholesterol-lipid metabolism, atherogenesis and development of coronary disease. The developing sex differential may be due to a poorer tolerance in men than women for high-fat, high-calorie diets and obesity. These habits of overeating may also be more common among men than among women.

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These possible alterations in dietetics were related to economic changes in the country, e.g., urbanization, industrialization, mechanization, and prosperity. As already indicated, it was generally felt that these developments were associated with less arduous work, less expenditure of physical energy, less large-muscle utilization. Men were tending more and more toward sedentary modes of life, both at work and recreation.

These socioeconomic developments were considered by several respondents to be of possible significance from another aspect for cardiovascular-renal and coronary disease in males. It was frequently stated that in recent decades the occupational situations of males tended to be associated with ever greater psychological stresses and strains. Mention was made of growing job tensions, insecurities, worries, frustrations, inhibitions, the competitive "fast pace" without letup as middle age progressed, etc. The possible effects of World War I and of the depression were noted. Attention was also called to increased use of tobacco and to greater exposure to noxious gases, e.g., gasoline fumes. All these factors were deemed to be operative to a far greater degree in men than in women. They were related to both coronary and hypertensive diseases. Most of the respondents did not attempt any explanation of the mechanism whereby these factors might operate to influence the development of these diseases.

What Are Possible Reasons for the Decline in Cardiovascular-renal Mortality in White Women From 1920 to 1947? It was noted by some respondents that this trend was the most impressive one recorded. It therefore merited particular attention. With respect to the specific disease processes involved, it was indcated that a sizable decline had almost certainly occurred in death rates due to infectious diseases affecting the cardiovascular-renal system. This was also true with respect to C-V-R diseases related to pregnancy. Decline in mortality rates due to rheumatic heart disease and the cardiovascular-renal "complications" of diabetes also probably contributed. Concomitantly, white women manifested no trend toward loss of their resistance to coronary disease. All these phenomena

together were apparently adequate to account for the over-all reduction in C-V-R death rates exhibited by white women from 1920 to 1947.

The respondents suggested several factors possibly responsible for these observations. It was recognized that the sex differential in susceptibility to coronary disease might be related to endogenous gonadal function, estrogenic versus androgenic. As already indicated, however, these per se could not account for a trend developing in so short a time as 27 years. Further, although attention was called to development of menopausal estrogen therapy during these decades, it was estimated that this practice was neither widespread nor prolonged enough to contribute greatly to the trend.

The emergence in the early 1920's of the slim figure fashion was noted as an important influence which probably had led to a considerable decline in obesity in white women. A marked difference was suggested in the developing dietetic habits of men and women.

In contrast to the expressed opinion that occupational, socioeconomic, and psychologic problems had intensified for men during this period, an opposite estimate was made for white women. It was felt that women had climbed up the economic and social ladder during these decades. New job opportunities had opened. By virtue of smaller families and mechanical aids, women had been liberated from prolonged, exhausting household drudgery. Moreover, with less childbearing and better medical care, there were fewer immediate risks in women with heart disease, as well as fewer long-term cardiovascular-renal sequelae. These socioeconomic and medical developments have probably contributed to lowering the incidence of cardiovascular-renal infections in women. Further, women—unlike men—were finding it possible more frequently to slow down at the ages of 40 to 60 years, with their children grown. It was also suggested that women's household duties, in becoming less arduous, may have moved from a harmful into a healthful range—whereas for many men the development had gone too far, i.e., to a deleterious lack of physical activity at work.

What Are Possible Reasons for the Nonwhite Cardiovascular-renal Mortality Trends? This particular problem received only limited treatment, since it was not posed in the original questions. A few respondents commented that nonwhite men may have less coronary disease than white men, even though over-all cardiovascular-renal mortality rates were higher in the former.

It was suggested that if this is the fact, it may be due to a lower standard of living in nonwhite men, with resultant heavier work and lower ingestion of expensive foods, e.g., fats—and with a resultant lower incidence of obesity. The higher over-all cardiovascular-renal death rates in nonwhites, and the failure of nonwhite women to exhibit the decline recorded for white women, were attributed in part to poorer medical care in the South and Southwest.

What Are Possible Avenues for Future Research on These Problems? A few respondents suggested further work with mortality data, including vital statistics and insurance company findings. Most of the proposals dealt with possible areas of epidemiologic research in living population groups. These included studies on a national and international scale correlating age-sex-race specific prevalence and incidence of coronary disease with population group patterns of diet, occupation,

habitual physical activity, personality, psychology, and others. Comparative analyses of disease prevalence and incidence were recommended in veterans versus nonveterans, obese versus nonobese, hypertensives versus normotensives, diabetics versus nondiabetics, housewives versus women in the labor force, urban versus rural dwellers, inhabitants of cities versus groups living in isolated special communities (e. g., agricultural, mining, or lumbering communities, with and without mechanization of the work processes).

CONCLUSION

The brief period of 5 years since these replies has been one of remarkable investigative activity on the problem of atherosclerosis and coronary disease—remarkable for both its range and achievement. Intensive research has proceeded, utilizing the three major methodologies—epidemiologic, clinical-pathologic, and animal-experimental. Many of the questions posed and projects recommended by the expert consultants have been undertaken, with significant results already available.[24] These embrace multiple facets of such problems as the interrelationships among dietary constituents, cholesterol-lipid-lipoprotein metabolism, atherogenesis, thrombogenesis and coronary disease; interrelationships between these parameters and heredity, nationality, race, occupation, income, place of residence, physical activity. Considerable information has been obtained on correlations between coronary disease incidence and obesity, hypertension, and smoking. Much fruitful work has been done on the influences of the gonadal hormones, particularly estrogens, on cholesterol-lipid-lipoprotein metabolism and atherogenesis. Attention has been focused on the problem of coronary disease and hypertension in nonwhites (Negroes, American Indians, Japanese- and Chinese-Americans). A beginning has been made on the problem (fraught with methodologic difficulties) of assessing the role of emotional factors, e.g., their effects on plasma cholesterol-lipid-lipoprotein levels and on clotting phenomena.

A critical analysis of the numerous recent studies is beyond the scope of this paper. Several excellent reviews and symposia are available, and these afford a comprehensive insight into the whole field.[16-24]

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SOCIOECONOMIC STATUS AND DIABETES MELLITUS

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ALL OF the etiologic factors in diabetes mellitus have not been ascertained. Diabetes mellitus may be defined therefore as a metabolic syndrome, involving unknown etiologic factors, which is usually not recognized until varying degrees of insulin insufficiency appear and in which certain manifestations can be controlled by regular and judicious use of food and insulin. The patient occupies the most important role in this type of control because he must judge his diet, take his insulin, and test his urine regularly and competently. To do this adequately, the patient must have a regular, constant supply of food, insulin, and urine testing materials of correct types and quantity and must receive adequate instruction in selection and preparation of food, administration of insulin, and the testing of urine. The patient must be capable of understanding these instructions and be mentally and physically capable of carrying them out.

The role of the physician is no less important[1] as he must have knowledge of (a) the principles of diet therapy and the ordering of diet containing proper amounts of potential dextrose, protein, and calories, (b) the types of insulin, their action curves, the indications and contraindications of each, (c) how to teach the patient to select and prepare the prescribed diet, to administer insulin, and to test the urine. The physician must also ask the appropriate questions and be able to counsel on problems that thus arise. He must be aware of the degenerative processes and complications that occur and search diligently for their presence; to do this properly, adequate time and facilities must be available. In considering these points it is easy to see that the average diabetic patient attending a large charity diabetic clinic will differ significantly from the average diabetic patient under private care. In an attempt to clarify and quantitate some of these factors, a study was instituted in 1955 in the Diabetic Clinic at Jefferson Davis Hospital, a City-County charity hospital. This clinic has 780 diabetic patients registered and meets one-half day per week with from 50 to 100 patients (average 70) in attendance. Three or four house physicians (one

This study was aided by a Training Grant, National Institute of Arthritis and Metabolic Disease, United States Public Health Service.

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or two residents and two or three interns) carry the bulk of the load in supplying medical care to these patients. Two registered nurses are available to supervise the general operation of the clinic, to keep the patients moving in and out, to give injections, to assist with examinations, and to give instructions on the administration of insulin and the testing of urine. One or two staff physicians are present to supervise the house staff, assist with the patient load, and carry out clinical research projects. One technician tests the urine for sugar and acetone before the patient is seen by the physician. One dietitian working on a voluntary basis is present to give dietary instruction and advice. One secretary and two volunteers help with the paper work. Eligibility to attend this clinic is determined by financial and residence status, with the financial requirements being the most important. A single person may have an income of no more than $100 per month and a couple no more than $125 per month to be eligible to attend this clinic. An added $20 income is allowed for each child up to a total of four children; therefore, the income ceiling for a family of 6 or more persons is $205. In contrast to these income ceilings, the patient who is totally dependent may receive grants of $30 to $45 per month from the local Board of Public Welfare. Twenty-four dollars of this is to cover rent and utilities, and the remainder is to be spent on food, clothing, and personal supplies. The consulting dietitian has worked out a set of diets which are designed to meet minimum nutrition requirements, conform to racial diet habits, and to be as inexpensive as possible. It has been calculated that this diet costs from $20 to $21 per month per person if the patient knows where and when to buy the food and how to prepare it properly. Social Service interviews of 180 patients revealed that 55 per cent of these patients had less than this minimum amount of money available to buy food. As a consequence the patients buy cheap foods which are mainly carbohydrate and fat. When the diet is high in carbohydrate there is usually an associated increase in fat intake in the forms of margarine, gravy, fried foods, and cuts of meat that are almost pure fat. The protein intake is low, and the incidence of obesity is quite high. This then becomes a type of vicious cycle; the high-carbohydrate, high-fat, low-protein diet is not satiating to the patient, who then eats more. With this there is an increase in weight, and the carbohydrate component of diabetic metabolic syndrome is more difficult to control. It is obvious that weight reduction and a high-protein diet would be beneficial to these patients, but these dietary goals are difficult to accomplish because of the socioeconomic conditions discussed above. In addition to these considerations there are other factors, such as the concept held by a large segment of the Negro population that some degree of obesity, especially in women, is a sign of good health. It is apparent that the social, economic, and intelligence level of this group of clinic patients is lower than that found in the general population. This decreases to a rather marked degree the ability of these patients to cooperate in the care of their diabetes.

Outpatient chart reviews and interviews have been carried out on 224 diabetic patients selected at random in the clinic. The reviews were performed by two physicians in a standardized manner. Table I gives the division of patients by race and sex. It is seen that Negro patients and women predominate. The

percentage of females is greater than reported from other clinics.[3,4] Fig. 1 shows the age group distribution, which agrees quite well with other reports.[3,4] Table II shows the distribution of patients according to the type of diabetes, as judged

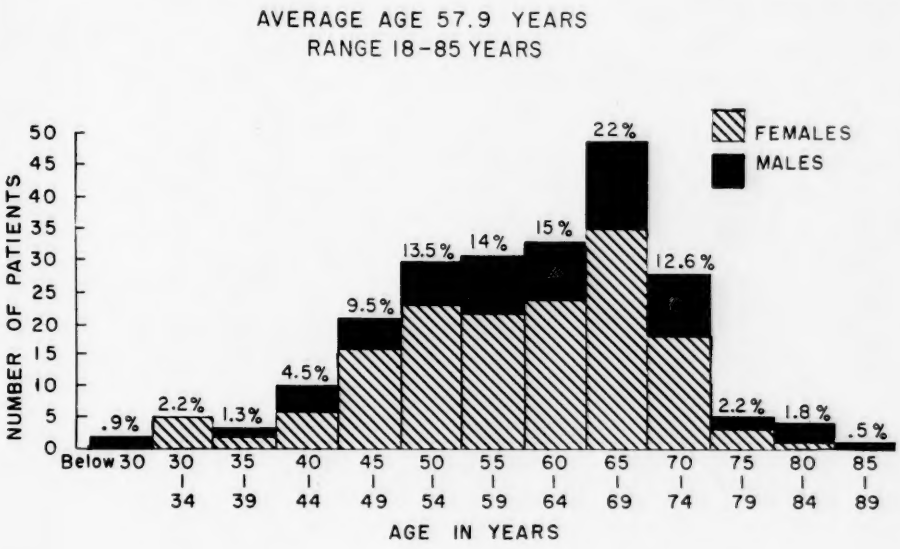

Fig. 1.—Age distribution.

TABLE I. DIABETIC PATIENTS

RACE	FEMALE	%	MALE	%	TOTAL	%
Negro	108	48	33	15	141	63
Latin American	6	3	5	2	11	5
White	47	21	25	11	72	32
Total	161	72	62	28	224	100

TABLE II. TYPES OF DIABETES

Adult	95.5%
Juvenile	3.1%
Endocrine	1.3%

by the information available. The juvenile type includes the brittle diabetics who, as a rule, develop their disease before the age of 20 years. The endocrine types include the diabetes associated with Cushing's syndrome, acromegaly, etc. Further investigation should give a further breakdown of the adult type of dia-

betes into subdivisions such as pancreatic, obesity, and arteriosclerotic.[5] In Fig. 2 is shown the duration of diabetes as determined from the date of diagnosis. The average duration is shorter than in other reports.[3] This may be due, in part, to relatively late diagnosis in our clinic.

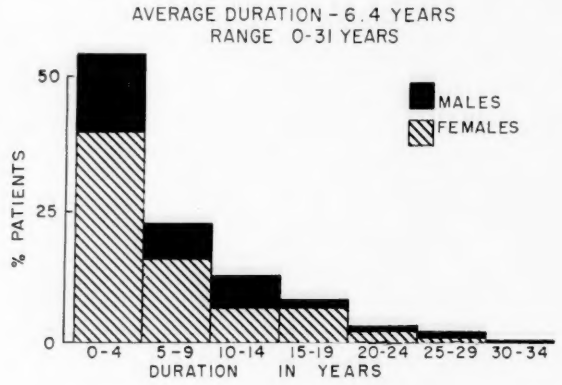

Fig. 2.—Duration of diabetes.

TABLE III. WEIGHT

	% WOMEN	% MEN	% TOTAL
Overweight	74	54	68
Normal	18	31	22
Underweight	5	10	7
Unknown	3	4	3

TABLE IV. DIETS

NO.	CALORIES	POTENTIAL DEXTROSE	PER CENT OF ALL PATIENTS	PER CENT OF ALL OVERWEIGHT PATIENTS		
				WOMEN	MEN	TOTAL
1	1755	243	52.3	48.0	52.8	49
2	2160	270	10.7	3.5	16.6	7
3	2350	306	4.5	1.7	2.8	2
4	1260	156	29.0	43.5	27.8	40
Special and unknown			3.5	3.5	0	2

The weight status of these patients is shown in Table III. The weight standards of the Metropolitan Life Insurance Company were used, and all patients whose weight fell within the normal ranges for their height were accepted as normal. Two-thirds of all patients were overweight, with a higher incidence in women than in men. The standardized diets used routinely in the clinic are shown in Table IV, as is the percentage of all patients on each diet and the per-

centage of overweight patients on each diet. As the number 1 diet provides normal caloric requirements for most women it is a bit surprising to find that one-half of the obese women are on this diet. One explanation is that the patients will not stay on a reduction diet, and therefore the house physician takes the line of least resistance and prescribes the diet which the patient is eating. Even more important is the fact that most of these apprentice physicians have little idea of the methods used to calculate a diet; therefore, it is worth while to consider the information and training the physician should have when he attempts to care for the diabetic patient.

The medical school curriculum is so condensed that only basic principles can be taught to the student. There is not enough time to teach the details which are extremely important factors in the satisfactory care of the diabetic. The embryo physician must depend on his hospital training to learn these all-important details. It is obvious that it is impossible to learn these or to perform even cursory examinations when the physician is confronted with the outpatient care of from 15 to 25 diabetics in a 3-hour period. Even if the senior staff has sufficient time and opportunity to teach, there is not enough time for the intern to partake of this instruction if he is to finish his work before the next clinic begins. As an inevitable consequence, cook book or set-routine medicine is practiced, with lesions and complications being picked up far too late for any effective therapy. Some of these difficulties are illustrated in the following discussion.

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TABLE V. TYPE OF INSULIN USED

	PRESENT STUDY (PER CENT)	BELLEVUE HOSPITAL (PER CENT)
NPH	69.2	0
PZI	12.9	14.0
Lente	1.8	0
Regular crystalline	0	30.0
Globin	0	0
Combinations	0	19.0
None	16.1	30.0

Table V shows the percentage of patients on each type of insulin in our clinic; comparable figures from one of the diabetic clinics at Bellevue Hospital[3] are also given. The smaller number of patients receiving no insulin in our series is probably due to several factors: (a) the feeling that even mild diabetics should receive insulin, (b) attempts to substitute insulin therapy for adequate patient training and habits, and (c) tendency toward increased glycosuria in our patients, especially in the obese patients, for reasons discussed above. In our series all patients on insulin therapy were receiving long-acting insulins in a single dose in the morning. It is well known that the long-acting modifications are extremely useful and that many patients do quite well on them, but in 224 patients it is certain that at least a few present unusual problems in therapy and should be placed on other insulin regimens. The failure to use globin insulin is unfortunate, since this is an excellent product, especially when divided doses are given.

Table VI shows the percentage of patients in each dosage range of insulin. All patients were receiving this dose in a single injection. It is now our feeling, as well as that of others,[6] that many patients receiving a daily dose of more than 60 units of the longer acting insulins should receive this in divided doses. The larger doses in a single injection often lead to the problem of alternating hyperglycemia and hypoglycemia, which may completely incapacitate the patient.

TABLE VI. INSULIN DOSAGE

None	16.1%
Less than 30 units	26.1%
30 units or more	42.0%
60 units or more	13.0%
100 units or more	1.8%

TABLE VII. CONTROL AS JUDGED BY GLYCOSURIA

Uncontrolled	11.6%
Poor	26.7%
Fair	20.1%
Good	25.9%
Excellent	15.6%

TABLE VIII. PHYSICAL EXAMINATION

	DIABETIC CLINIC	GENERAL CLINIC
None or inadequate	11%	4.4%
Last PX is hospital discharge summary	12%	2.9%
20 months or longer with no adequate PX	24%	7.4%
Average duration since last PX	13.2 mo.	7.0 mo.
Longest period	63 mo.	79 mo.

In this type of care the main concern is to control the glycosuria and prevent ketonuria to the virtual exclusion of other considerations. In other words, the blood sugar determinations and urine tests are being treated, not the patient. Yet the control of the diabetes, as judged by the degree of glycosuria, is not good, as is shown in Table VII. If a little time is spent in talking with the patients, it is readily apparent that many have irregular habits, varying the time that they take their insulin and eat their meals, as well as varying the quantity and quality of food eaten. This accounts for most of the difficulty resulting in poor control and increased glycosuria.

A reflection of the overcrowding and understaffing in this clinic is the status of the patients with regard to physical examination. In Table VIII it is seen that one-tenth of the patients have had no adequate physical examination recorded

in the outpatient chart and that another 12 per cent had their last physical performed as inpatients. For purposes of this study the recording of an examination of the heart, lungs, abdomen, and vital signs was accepted as adequate (which obviously is not true in many instances). For comparison is shown the status of 205 patients attending the general Medical Clinic in the same hospital. In comparing the statistics it should be noted that every attempt is made to see all diabetic patients at least twice a year. Patients followed in the general clinic are seen only as indicated, and in many instances there is a period of years between visits; lapses of 10 years are not uncommon. In the diabetic clinic the physician sees about 6 patients per hour; in the general clinic he sees about 4 patients per hour.

TABLE IX. URINALYSIS

	DIABETIC CLINIC	GENERAL CLINIC
No complete urinalysis is recorded	10%	3%
> 29 months since complete urinalysis	20%	9%
> 39 months since complete urinalysis	14%	6%
> 49 months since complete urinalysis	9%	5%
Longest period with no complete urinalysis	80 mo.	118 mo
Average duration since last complete urinalysis		
All patients	18.5 mo.	8.5 mo.
Patients with abnormalities in last urinalysis	17.5 mo.	8.7 mo.
Abnormalities on last urinalysis		
Abnormal	48%	39%
Cellular elements	23%	19%
Proteinuria	23%	19%
Both	8%	9%

TABLE X. CHEST X-RAY

	DIABETIC CLINIC	GENERAL CLINIC
No chest x-ray	16.5%	12.6%
> 19 months since last chest film	20.0%	21.0%
Average period since last film	14.4 mo.	11.6 mo.
Longest period	91.0 mo.	63.0 mo.

It is well known that the genitourinary system is frequently involved by any of several processes in diabetes, yet there is a marked tendency to overlook the periodic performance of complete urinalysis, in spite of the fact that analysis for sugar and acetone are done quite religiously at each clinic visit. This is clearly shown in Table IX, as is the fact that little attention was paid to the presence of abnormal quantities of cellular elements, or to the presence of proteinuria.

This can only mean that the attention of the staff was focused on the urine sugar, and there was a failure to appreciate the significance of urinary tract abnormalities.

As might be anticipated, the incidence of degenerative disease and complications is quite high in a clinic diabetic population existing under these socioeconomic and medical conditions. Table XI illustrates the incidence of complications as judged by this review. A more complete report on this aspect is in preparation.

It is quite obvious that these are problems faced by all physicians involved in rendering professional care to diabetics. It is also evident that the role played by the house staff physicians under our present system of education and training is somewhat precarious. The physicians trained in these hospitals today are the practitioners of tomorrow. It is also felt that these problems are not isolated to this particular clinic. As contact has been made with various charity diabetic clinics over the country, it appears that the same basic problems exist in almost all of these charity clinics.

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TABLE XI. DEGENERATIVE DISEASE AND COMPLICATIONS

Cataracts	20.0%
Hypertension	
Mild	34.0%
Moderate	9.5%
Severe	0.9%
Heart disease	39.0%
Taking digitalis	17.0%
Neuropathy	
Suspected	22.0%
Diagnosed	13.0%
Diarrhea	13.0%
Symptomatic arteriosclerosis	55.0%
Foot infection	16.0%
Gangrene	8.5%
Amputation	7.5%
Positive family history	26.8%

CORRECTIVE MEASURES

This study was undertaken to document the problems that were known to exist in this clinic. At the conclusion of the study certain corrective measures were instituted. It was not possible to increase the number of house staff physicians assigned to this clinic, but it was possible to utilize the services of the medical students to perform complete medical work-ups, and about one-fourth of the patients receive this service each year. In addition, a routine has been established so that chest x-rays and electrocardiograms are obtained periodically and each urine is now analyzed for sugar, acetone, protein and cellular components. A training program has been established in which an attempt is being made to teach each diabetic attending the clinic more about the disease. A chiropody

section has been added to the diabetic clinic so that all patients are instructed in foot care and problem cases receive special attention. A vascular surgeon attends all clinics to help with the problems in his field. A social worker has been added to the staff and her services are invaluable in a multitude of ways. A Public Health nurse has been assigned to the hospital to teach the student nurses to give proper nursing care and instructions to diabetic patients. Much of this instruction is given in the clinic where the student nurses, under the supervision of the instructor, teach the diabetic patients the proper methods of administration of insulin and testing of the urine. The size of the senior staff has been increased. Last, but far from least, the house staff is being taught to consider the diabetic as a patient, not as a problem in glycosuria.

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SUMMARY

The diabetic patient attending a charity clinic presents a multitude of social, economic, and medical factors that tend to make him a much different problem from the diabetic under private care. These charity patients are faced with extremely limited financial resources, are on the average in a lower intelligence group, and are often given rather superficial medical care. All too often, there is more interest in the urine or blood sugar than in the patient. Some of the measures employed to correct the more serious problems are discussed briefly.

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AN EPIDEMIOLOGIC STUDY OF THE NEPHROTIC SYNDROME

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THE incidence of the nephrotic syndrome has never reached epidemic proportions. However, methods used by the epidemiologist are helpful for the "study of the distribution of a disease or a condition in a population and the factors that influence this distribution," as Lilienfeld[1] has defined this approach. According to Lilienfeld,[1] the study of the variations in frequency of diseases by such characteristics as age, sex, race, social class, and occupation may modify existing hypotheses or permit development of new hypotheses. It was thought fruitful to determine age, sex distribution, and other characteristics in a group of patients with the nephrotic syndrome, in a search for possible statistical associations between the disease and various demographic characteristics. For this purpose, data were collected from all pediatric departments of hospitals in the Greater Buffalo area that had admitted nephrotic children in the period 1940 through 1956. An interesting difference in the sex distribution was noted between nephrotic children who resided within the city limits and those who resided outside the city limits; this difference was considered of sufficient importance to warrant reporting.

Data regarding the age and sex distribution of a large number of nephrotic children had been obtained previously by Barness and co-workers.[2] The mean age at onset was 3.5 ± 2.1 years, and the ratio of male to female patients was 1.6 to 1 in their series of 151 patients. Regarding the incidence of nephrotic children, Rothenberg and Heymann[3] estimated the number of new cases per 100,000 children 0 through 9 years old to be 6.9 per year for Greater Cleveland and 2.3 per year for Ohio. The incidence in the nonwhite population of Ohio was calculated to be 3.2 per 100,000 per year.

METHOD OF STUDY

Several assumptions had to be made for the purpose of this study.

1. The occurrence of the nephrotic syndrome in a child is dramatic enough to warrant hospitalization.

2. The first hospitalization occurs usually in a hospital near the patient's home.

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3. The symptoms of the nephrotic syndrome in a child are usually typical enough to lead to adequate investigation of the disease process. Detailed laboratory data will then be available in the patient's hospital records, and, in the majority of cases, a correct diagnosis is made.

4. The records of almost all cases of nephrotic syndrome are filed in hospital record rooms under "nephrotic syndrome," "nephrosis," "lipoid nephrosis," or "chronic glomerulonephritis."

All record librarians of the hospitals of the Greater Buffalo area were kind enough to provide a list of records filed under the headings just mentioned. All records were reviewed personally, and the diagnosis of nephrotic syndrome was verified by using the accepted criteria: edema, proteinuria, hypoproteinemia, hypercholesterolemia, and absence of a history of preceding acute glomerulonephritis. From these patients, the following data were recorded: age in years and months at the time of onset; sex; race; month and year during which the first swelling was noticed; occupation of the father of the patient; and age and number of siblings. No follow-up study was attempted.

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The patient's residence at the time of onset of the disease was plotted on a map of Erie County. On this map, the area of the city of Buffalo was subdivided into 72 census tracts which had been used for the Seventh Decennial Census conducted as of April 1, 1950. The census-tract statistics obtained at that time were utilized for this study regarding population, racial distribution, and socioeconomic status.[4] All figures obtained in 1950 could be used for the whole period of this survey since there was only a minimal change in the population of Buffalo from 1940 to 1950, namely an increase from 575,901 to 580,132.

RESULTS

The record librarians of the cooperating hospitals supplied lists totaling 160 patients. All cases of acute glomerulonephritis, lower-nephron nephrosis, and other conditions not meeting the criteria of the nephrotic syndrome were eliminated. Duplicates due to admission of the same patient to different hospitals during the course of his illness were also not considered. Seventy-two patients, or 45 per cent of the original number, remained for analysis.

Of these 72 patients, 37 were living within the city limits at the time of onset of symptoms, while the other 35 patients had their residence in the suburbs or were referred from a nearby town (five of the 35 patients).

The mean age of these 72 patients was 4.26 years; however, the age distribution was skewed (Fig. 1). Almost half of these children (34) were less than 4 years old, and the frequency of occurrence was highest among children 1 and 2 years old. The ratio of males to females in the whole group was 1.9 to 1. Fig. 2 shows the distribution of patients according to month of onset, and Fig. 3 according to year of onset. The number of new cases per year shows some fluctuation but no epidemic accumulation. The onset of swelling was more often noted in the spring and in the fall, but the number of cases is too small to allow any statistical correlation regarding seasonal variations.

It was possible to calculate the incidence of the nephrotic syndrome within the city limits of Buffalo since adequate demographic data were available. For

reasons of comparability with Rothenberg and Heymann's data, the calculation was carried out for children 0 through 9 years old (Table I) over the 17-year period represented by this study.

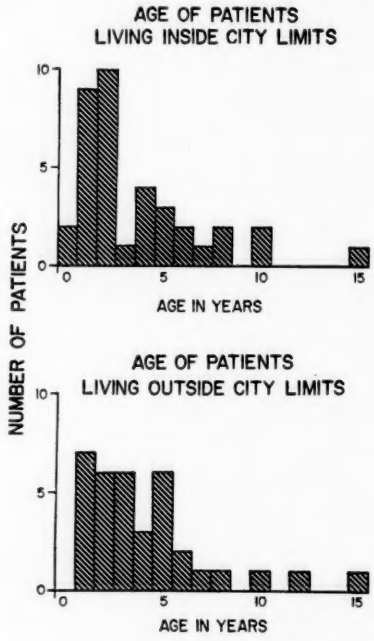

Fig. 1. Age distribution of patients living inside and outside the city limits of Buffalo.

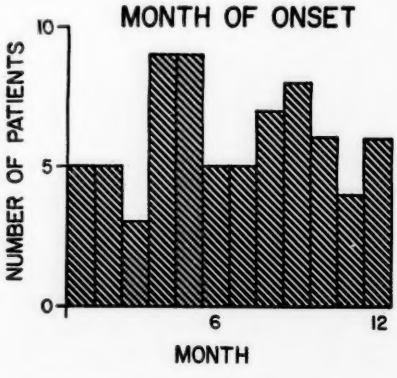

Fig. 2. Distribution of patients according to month of onset of edema.

The incidence of the nephrotic syndrome did not appear to be greater in any particular sector of the city. There was not a single instance in which more

than one case of the syndrome was detected in the same year and census tract. It was interesting to note, however, that cases occurred in only 27 census tracts out of a total of 72. In certain large areas of the city, no case of the syndrome

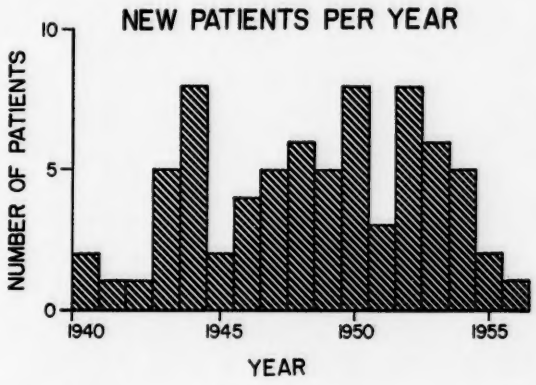

Fig. 3. Distribution of patients according to year of onset.

TABLE I. INCIDENCE PER 100,000 CHILDREN (0 THROUGH 9 YEARS OLD) PER YEAR

	MALE	FEMALE	BOTH SEXES
White	2.9 (22)*	0.82 (6)	1.9 (28)
Nonwhite	9.8 (6)	0	4.8 (6)
All children	3.4 (28)	0.75 (6)	2.1 (34)

*Numbers in parentheses are total numbers of cases in 17-year period.

TABLE II. DISTRIBUTION OF PATIENTS ACCORDING TO SOCIOECONOMIC QUARTILE

QUARTILE	PATIENTS
1 (high)	9
2	7
3	12
4 (low)	9

could be found. The 72 census tracts were subdivided into four quartiles according to their socioeconomic status. This division was based upon the median contract monthly rent of each census tract. The quartile distribution of patients with the nephrotic syndrome is shown in Table II. No significant difference was

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demonstrable. It was attempted to correlate incidence per census tract with median yearly income and with median completed school years. However, no correlation could be found.

The occupation of the father was evident from the patient's record in 20 instances. The occupational distribution of fathers of nephrotic children was compared with the occupational distribution of the general population in Buffalo (Table III). No significant differences were noted, but the small numbers do not allow a definite conclusion.

TABLE III. OCCUPATIONAL DISTRIBUTION OF FATHERS OF NEPHROTIC CHILDREN COMPARED WITH OCCUPATIONAL DISTRIBUTION OF GENERAL POPULATION OF BUFFALO

OCCUPATION	OCCUPATIONAL DISTRIBUTION, PER CENT	
	FATHERS OF PATIENTS	GENERAL POPULATION
Professional, technical, and kindred workers	5 (1)*	7.6
Managers, officials, and proprietors, including farm	5 (1)	10.4
Clerical workers	10 (2)	8.3
Sales workers	15 (3)	6.2
Craftsmen and foremen	25 (5)	24.1
Operatives and kindred workers	15 (3)	24.8
Service workers	15 (3)	7.6
Laborers	10 (2)	10.0

*Numbers in parentheses are numbers of cases.

The group of nephrotic children living inside the city was compared with the group living outside (Table IV). Both groups appear rather homogeneous with one significant exception. The sex ratio of cases within the city limits (31 male to 6 female) was considerably different from that of cases outside the city limits (16 male to 19 female). If 47 male and 25 female patients had been randomly allocated so that 36 cases would appear in the city and 36 outside, the probability of getting a proportion of males to females as high as or higher than that actually observed outside the city would be less than 0.002. The method for determining this probability was the normal approximation to the hypergeometric distribution.

No cases among nonwhite children were found among the children living outside the city limits, but this is explained by the fact that very few nonwhite people reside outside the city limits.

COMMENT

This survey has obvious shortcomings. One is due to the fact that it is concerned with hospital population only. There may be many subclinical cases

of the nephrotic syndrome in which a diagnosis was never made for lack of symptoms. Only screening of a large population with urinalyses could correct this deficiency. Such screening poses problems. The second deficiency can be seen in the fact that not enough patients could be included for a more detailed analysis.

New cases of the nephrotic syndrome among children up to and including the age of 9 years occurred during 1940 through 1956 at a rate of 2.1 per 100,000 children per year. This figure is lower than the incidence reported for the Greater Cleveland area but approximates Rothenberg and Heymann's figures for Ohio. It may be that these authors' Cleveland figures included many patients in whom the diagnosis would not have been confirmed by individual review of their hospital records. The observation in the Ohio study that the nephrotic syndrome occurs more frequently among nonwhites seemed to be verified in the present study. However, the total figure of 6 patients in this study is too low to allow an exact calculation of incidence for the nonwhite population.

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TABLE IV. SEX, RACE, AGE, AND SIZE OF FAMILY OF PATIENTS LIVING INSIDE AND OUTSIDE CITY LIMITS

	INSIDE CITY LIMITS	OUTSIDE CITY LIMITS
Total patients	37	35
Admitted to Children's Hospital	27	27
In other hospitals	10	8
Male	*31*	*16*
Female	*6*	*19*
White	31	35
Negro	5	0
Indian	1	0
Mean age, years	4.0	4.6
Median age, years	2 10/12	3 8/12
Patient first born, per cent	51.8	53.8
second born, per cent	22.3	26.9
third born, per cent	11.1	11.5
fourth born, per cent	11.1	3.9
fifth born, per cent	3.7	0
sixth born, per cent	0	3.9

The only remarkable finding was the difference between the sex ratio of afflicted children living within the city limits and the sex ratio of children living in the suburbs. Sampling selection appears to be unlikely to explain this difference since there is no reason to believe that girls from the suburbs who have ne-

phrotic syndrome are transferred more often than boys to a hospital in the city. It is equally unlikely that this syndrome is diagnosed more often among boys than among girls within the city limits. Nevertheless, only the confirmation of this finding in other cities would allow definite conclusions.

An explanation of this phenomenon may be found in a difference in exposure between boys and girls living within the city limits to a disease-producing factor, in contrast to equal exposure outside the city limits. The low incidence points out that this occurs most infrequently, and the age incidence would indicate that such an exposure would occur most often in children between 1 and 2 years old. But the results of this study would not even allow a guess as to the exact nature of this factor.

SUMMARY

Epidemiologic methods were used for a survey of nephrotic children admitted to the hospitals in the Greater Buffalo area. The incidence was found to be 2.1 cases per 100,000 children 0 through 9 years old per year. A higher incidence was found among nonwhite children. The sex ratio of nephrotic children living inside the city limits was very significantly different from that of nephrotic children living outside the city limits. On the basis of this study, a disease-producing factor is suspected in the patients' environment to which boys between 1 and 2 years old are exposed more often than girls who live within the city of Buffalo, while boys and girls are exposed equally often when they live in the suburbs or smaller towns.

Dr. Abraham M. Lilienfeld, Chief of the Department of Statistics and Epidemiology of the Roswell Park Memorial Institute, offered many helpful suggestions for the preparation of this report.

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EXPERIENCE IN THE MANAGEMENT OF JOINT AND SOFT TISSUE DISEASE WITH A NEW FORM OF HYDROCORTISONE FOR LOCAL INJECTION

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THE search for effective agents for control and alleviation of symptoms and signs secondary to disease of joints and bursae has in recent years centered about the use of local modalities. Following the initial enthusiasm for systemic steroid therapy and the subsequent realization of the limitations and dangers of this class of drugs, an attempt to control local processes by the administration of drugs at the site of disease has been made, and many different compounds have been studied in this regard. Intra-articular procedures have been used for many years in relieving increased intrasynovial pressure by joint paracentesis and also for the administration of antibiotics in cases of joint infection. The use of intra-articular steroids on a large scale began in 1951,[1] when relatively large quantities of hydrocortisone became available. Before that time, cortisone had been studied and had been found relatively ineffective. With intra-articular hydrocortisone, responses were elicited comparable to or superior to the response obtained by oral or parenteral use of this compound. Brown and associates[1] reported, in a comparative assay of intra-articular cortisone acetate and hydrocortisone acetate utilizing various objective methods of measurement, a marked superiority for hydrocortisone in intensity, duration of activity, and consistency of local antirheumatic effect.

Hollander[2] based his evaluation of intra-articular injection effect on the following criteria: (a) measurement of joint circumference, (b) local tenderness, (c) range of joint motion, (d) synovial fluid cell count, and (e) joint temperature. He felt that beneficial results were due to the suppression of a local reaction to an irritant.

Many studies have been reported and others are in progress, attempting to determine the mechanism of effect of local steroid therapy and the fate of such steroid after administration. Zacco and his colleagues[3] studied the concentration of hormones in the synovial fluid, the distribution between cells and fluid at

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various intervals after intra-articular injection, and the rate of hydrolysis of the acetate esters of hydrocortisone and cortisone. The concentration of 17-hydroxy-corticoids in the joint fluid decreased at the same speed for all preparations. The 17-hydroxy-corticoid concentration in the synovial cells was highest after hydrocortisone acetate, less with cortisone, and hydrocortisone (free-form) was present only in the synovial fluid. They concluded that these studies did not explain the superiority of hydrocortisone acetate esters and free hydrocortisone compared to cortisone. Hollander[4] reported that injected microcrystals of hydrocortisone disappear in two hours from the synovial fluid and make their way into the lining cells of the synovial membrane where they are retained; he felt that hydrocortisone, being less soluble than cortisone in plasma, remained in the local area longer. Duff[5] described a reversion of the abnormal characteristics of synovial fluid to a more normal pattern after hydrocortisone administration. He felt that this effect was exerted at a connective tissue level and stated that the improvement in physical characteristics of the fluid could be attributed to an alteration in the polysaccharide component, hyaluronic acid. In studying response of joint fluid to intra-articular therapy, he found an increase in relative viscosity, a decrease in the number of nucleated cells, an increase in concentration of polysaccharide, and an increase in the percentage of good to excellent mucin clot formation (74 per cent to 97 per cent). A definite correlation was described between the clinical effectiveness of hydrocortisone injection and the reversion of joint fluid characteristics to a more normal pattern, although some dissociation of these variables was also noted. Repeated injections tended to produce a progressive change in joint fluid characteristics.

Hollander and Moore[6] indicated that the intra-articular temperature of osteoarthritic joints may be elevated after hydrocortisone administration, unlike the temperature response in rheumatoid joints. They felt that this might be due to an increase in blood flow in the joint. Hollander and Moore found that the temperature response to therapy was variable and concluded that relief of pain and stiffness was not directly related to intra-articular temperature change. Oka,[7] in studying the absorption of hydrocortisone from the joint into the circulation, stated that in some studies 21 per cent of patients showed systemic steroid effects after intra-articular administration. He pointed out that several workers had shown that hydrocortisone disappeared from the synovial fluid rapidly and that after 1 and 3 hours, respectively, 86 per cent and 97 per cent had disappeared. Thirty minutes after intra-articular administration, some hydrocortisone was found in the contralateral joint. He measured the plasma level of 17-hydroxy-corticosteroids under conditions in which the endogenous output of hydrocortisone had been eliminated and had obtained high levels after the intra-articular administration of 25 to 100 mg. hydrocortisone. The highest level was noted 3 hours after administration, fell to normal in 24 hours, and was equivalent to that produced by the oral administration of 25 mg. of hydrocortisone.

In another study, Duff[8] noted a decrease in the rate of accumulation of joint fluid after intra-articular hydrocortisone and a fairly good correlation between clinical results and joint fluid improvement, although synovial biopsies showed no change in the rheumatoid picture. He did not observe any systemic effects from local administration.

Dal Cortivo, Patterson, and Umberger[9] determined hydrocortisone levels in synovial fluid. They administered 50 to 75 mg. of hydrocortisone into the joint and removed fluid periodically. A rapid decrease in concentration of steroid in the fluid was noted, with little residual after one hour. Clinical improvement was correlated with rapidity of disappearance of hydrocortisone from the joint fluid. They felt that the rapid rate of disappearance was too great to be accounted for by simple diffusion across the synovial membrane. Miner[10] quoted studies by Ziff and associates in which chromatographic analysis was used in following the fate of administered steroids. After 3 hours, 97 per cent of cortisone and hydrocortisone disappeared. Metabolites found locally indicated their local formation after hydrocortisone absorption (these were not present in the opposite knee and were not found in normal synovial fluid after addition of hydrocortisone). The contralateral knee contained 0.1 per cent of the amount of hydrocortisone originally administered. The conclusion of Ziff and co-workers was that synovial tissue has enzymes capable of altering the steroid molecule. A sequence of metabolic reactions was postulated to occur from ½ to 3 hours after injection. The finding of hydrocortisone in the opposite knee showed that a proportion of the injected hormone entered the circulation unchanged and escaped metabolism in the liver during the first 30 minutes after injection. In explaining the difference in response to cortisone and hydrocortisone, they stated that both hormones were transformed into other products, and that synovial tissue can better form these products from hydrocortisone than cortisone. They further postulated that cortisone may be ineffective even though it is partially converted to hydrocortisone because the latter is not further transformed to the requisite metabolite. Three hours after administration of hydrocortisone, a metabolite accumulated in synovial fluid in an amount twice as great as that of the unchanged hydrocortisone.

In a recent exhibit by Hollander and associates[11] illustrating the fate of intra-articular hydrocortisone esters or analogs, it was stated that the steroid almost completely disappears from the joint fluid within 2 hours and the remainder is in a metabolized form. Some of the hormone reaches the systemic circulation, and this phenomenon is increased with a larger original dose; some of the steroid can be recovered from the synovial cells 48 hours after injection; and considerable steroid can be extracted from the biopsied synovial membrane 2 to 10 days after injection. He stated that hydrocortisone acetate disappeared from synovial tissue more rapidly (4 to 6 days) than hydrocortisone tertiary-butyl-acetate (TBA) (7 to 10 days).

Among the compounds currently being administered directly into joints, hydrocortisone acetate, hydrocortisone TBA, prednisolone, and prednisolone TBA are the effective forms. This paper will detail the use of another compound, hydrocortisone in concentrated form (150 to 200 mg./c.c.).

Indications for intra-articular administration of steroids are indicated in the following table taken from an A.M.A. exhibit[11]:

A. *Rheumatoid arthritis*
One of few peripheral joints being actively inflamed
When other steroids or gold salts are contraindicated

To suppress inflammation until gold or steroids become effective
To suppress resistant inflammation in a few joints when most joints are controlled by moderate oral doses of steroids
To prevent contractures and assist physiotherapy and manipulation
To control the bursitis or tenosynovitis accompanying joint inflammation

B. *Bursitis and tenosynovitis*
C. *Osteoarthritis*
To control acutely painful Heberden nodes
Symptomatic relief, particularly knee, hip, temporomandibular joint
D. *Traumatic arthritis*
E. *Gouty arthritis*
For localized joint swelling, acute and chronic
F. *In conjunction with orthopedic surgery or intensive physical therapy*
G. *Dupuytren's contracture*
H. *Extra-articular disease, i.e., fibrositis*

Contraindications to local steroid therapy include infectious arthritis (although in this series, several such cases were successfully treated by a combination of concentrated hydrocortisone and Neomycin) and spinal arthritis, although several papers have appeared recently describing techniques and indications for vertebral joint therapy. Kaplan[12] has reported six instances of septic arthritis after intra-articular administration. These cases required parenteral and local antibiotics plus immobilization for therapy. This investigator stressed the need for sterile techniques.

Preparation of the joint and modes of administration have been repeatedly described in many reviews, and no particular deviations from these accepted practices were utilized in this study. Knees were approached from the anteromedial aspect as were ankles; shoulders were approached from anterior, lateral, and posterior aspects; hips were injected from the lateral aspect primarily; elbows lateral to the olecranon; and wrists dorsally distal to the radius. Paravertebral injections were done according to the method described by Cohen, Rose, and Seven,[13] in which the needle is inserted into the skin just posterior to the mid-point of the lateral aspect of the neck at the level of the involved vertebra (determined by x-ray and palpation), then advanced medially and posteriorly at an angle of 45 degrees until the transverse process is encountered, and then directed toward the midline. When resistance is met, the area is infiltrated. A similar, though more posterior, approach is utilized for thoracic and lumbar vertebrae. With regard to extra-articular injection, Lipow, Kron, and Smith[14] summarized the techniques with illustrations of injection of extra-articular disease areas, with particular reference to trigger zones governing reference areas of pain elsewhere. Technique for intradiscal injection has been described by Feffer[15] under direct x-ray visualization.

Ziff, Contreras, and Schmid[16] have recently described the use of the hypospray jet injector in the local administration of hydrocortisone. Measured amounts of liquid are injected in a jet stream by a spring-activated plunger as the instrument is held firmly against the joint. Efficacy was tested by recovery

of material or dye from the joint cavity. Only side effects noted were initial burning and occasionally postinjection pain; a few instances of minor ecchymoses were reported. The technique has the disadvantage of not allowing joint fluid removal and is ineffective in the hip joint. Best results were obtained in hand joints.

In an attempt to increase duration of effect, the tertiary-butyl-acetate form (TBA) of both hydrocortisone and prednisolone has been employed, but there is still disagreement as to the extent of further improvement afforded. Hollander and associates[17] in a comparison of the effects of hydrocortisone acetate with hydrocortisone TBA reported that the compounds were equally effective in 90 per cent of 171 patients. However, the period of palliation was longer in 60 per cent with the less soluble TBA, equal for both drugs in 35 per cent, and longer in 5 per cent with the acetate. They feel that when the acetate is or becomes ineffective, the use of the tertiary-butyl-acetate is indicated. On the other hand, Zuckner, Machek, and Ahern[18] studied 38 patients and observed no appreciable difference between acetate and TBA. Duff[5,8] tested prednisolone TBA without finding any advantage over acetate, but in another series he found a slightly greater duration of effect with hydrocortisone TBA, averaging 11 to 20 days, as compared to 4 to 10 days with the acetate.

Significant relief of symptoms for varying periods of time has been reported by many observers with the use of intra-articular steroids. Boland[19] reported, in the early use of intra-articular steroids, an 80 per cent incidence of improvement although marked improvement was present in only 50 per cent. Sevastano[20] reported a total of 1,072 patients receiving a total of 6,423 injections with generally good results (80 per cent) and no instances of infection. Duff reported 50 per cent good results in a series of 60 patients receiving a total of 1,000 injections, and felt that considerable value was shown in the treatment of soft tissue lesions. Sacks[21] reported on 485 patients receiving about 1,000 injections and described 75 per cent good results in degenerative arthritis with the knees showing most marked results, and 58 per cent good results in rheumatoid arthritis (though less lasting than in osteoarthritis). In epicondylitis, he described 80 per cent good results, but only fair results in shoulder lesions. Hollander,[22] who has had extensive experience with this form of therapy, reported, in 1953, on 852 patients receiving over 8,000 injections, and described 85 per cent successful results (unequivocal improvement for at least 3 days) in both rheumatoid and hypertrophic arthritis, excluding the hip joint; 58 per cent good results in bursitis; and better than 90 per cent improvement in traumatic lesions. Only 20 per cent had sustained improvement. Poorest results were in chronic shoulder and hip lesions, and 2.3 per cent incidence of untoward effects were described (usually a transient exacerbation of joint pain). Only two instances of mild infection were reported. In the 1957 American Medical Association exhibit, Hollander and his colleagues[11] reported on the first 10,000 injections in 1,000 patients with similar statistics to those cited above but with permanent success in better than 50 per cent of 547 patients. Adverse reactions were of the same order as in the 1953 report. A 5-year follow-up of therapy of rheumatoid knees showed 31 of 100 patients no longer requiring intra-articular therapy and an

additional 48 receiving periodic injections with benefit (half of the latter now receiving the TBA ester) while in a similar follow-up of 100 cases of osteoarthritis of the knee, 59 patients no longer need therapy and 14 continue to receive periodic treatments with relief. Lipow, Kron, and Smith,[14] using prednisolone TBA, cite better than 90 per cent good results in acute bursitis and sprain, with a shorter duration of disability as compared to conventional therapy or oral steroids.

Steinbrocker and Neustadt[23] studied intra-articular phenylbutazone in 33 patients with varied forms of arthritis and rheumatic disease. He used a 20 per cent solution at 2-week intervals and noted favorable results particularly in acutely swollen joints, with improvement in synovial fluid being correlated with clinical improvement. He stated that therapeutic results were similar to those previously reported for intra-articular hydrocortisone.

METHODS

In an attempt to improve further the efficacy or duration of response of intra-articular therapy, this study has been undertaken with some new preparations of hydrocortisone, containing 150 and 200 mg./c.c. In addition, in selected cases, a compound containing 50 mg./c.c. hydrocortisone combined with Neomycin 5 mg./c.c. was employed. Technique of administration, preparation of joint for injection, and mode of evaluation of results was essentially similar to that described in the many studies cited previously. An average dose of 1.0 c.c. was administered in most joints.

Because of the concentration of the fluid used, it was found more convenient to use needles of No. 22 or larger, although occasionally injections were given through No. 23 needles, particularly when procaine was also used. It was necessary to inject the fluid fairly rapidly after filling the syringe when using the 200 mg./c.c. concentration without procaine to avoid obstruction of the needle bore. With the 150 mg./c.c. concentration, no such difficulty was encountered.

Results were evaluated both subjectively, according to relief of pain and stiffness, and objectively by joint circumference measurement, range of motion, tendency to recurrence of effusion, and local tenderness by palpation. The same joint was evaluated when possible by comparing the effect of usual forms of hydrocortisone (50 mg./c.c.) with the effect of concentrated hydrocortisone, or by comparison of two analogous joints (e.g., both knees when affected with a similar lesion) by using a different form of hydrocortisone on each side. In most instances, other forms of therapy had been utilized to their maximum advantage. Most joints or bursae had received physiotherapy; some joints or bursae had had prior x-ray therapy. In few cases of traumatic arthritis or bursitis, C-reactive protein reactions were studied prior to and following intra-articular therapy.

Side effects looked for included local joint or bursal reaction and systemic steroidal reactions such as change in blood pressure, weight gain, appearance of edema, development of gastrointestinal symptoms, change in sugar levels in diabetics, and cerebral symptoms such as headache, irritability, euphoria, etc.

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TABLE I. THERAPEUTIC EFFECTS

LOCATION OF DISEASE	NO. OF CASES	TYPE OF DISEASE	DURATION OF SYMPTOMS*	PRIOR THERAPY*	RESULTS*			
					SUBJECTIVE			OBJECTIVE
								RANGE OF MOTION
					N	M	E	BEFORE → AFTER
Hip	2	Osteoarthritis	Chronic	Physiotherapy	1	1	0	60°F → 90°F
Cervical spine	2	Osteoarthritis	Chronic	Physiotherapy, x-ray	1	1	0	30°F → 50°F 20°Ex → 35°Ex
Lumbar spine	1	Disc disease	Chronic	Physiotherapy, traction	0	1	0	25% increase
Wrist	3	Tenosynovitis	Chronic	Physiotherapy, surgery	0	2	1	50% increase
Ankle	6	3 rheumatoid arthritis	2 acute	Physiotherapy, oral steroid	0	2	0	50% increase
			1 chronic	Physiotherapy	1	0	0	No change
		3 trauma (chronic sprain)	Chronic	Physiotherapy	0	3	0	50% increase
Elbow	5	2 rheumatoid arthritis	Chronic	Physiotherapy, oral steroid	0	2	0	50°F → 40°F 150°Ex → 175°Ex
		3 epicondylitis	1 acute	Physiotherapy, phenylbutazone	0	0	1	60°F → 30°F 100°Ex → 180°Ex
			2 chronic	Physiotherapy	0	2	0	50°F → 40°F 140°Ex → 160°Ex
Shoulder	15	2 rheumatoid arthritis	Chronic	Oral steroid	0	1	1	90° abd → 165° abd
		2 osteoarthritis	Chronic	Physiotherapy	1	1	0	110° abd → 140° abd
		11 bursitis	4 acute	Physiotherapy, oral steroid	1	2	1	90° abd → 160° abd
			7 chronic	Physiotherapy, x-ray	2	3	2	120° abd → 150° abd
Knee	22	12 rheumatoid arthritis	3 acute	Physiotherapy, oral steroid	0	2	1	60°F → 45°F 150°Ex → 180°Ex
			9 chronic	Physiotherapy, steroid, and phenylbutazone	2	5	2	60°F → 45°F 150°Ex → 170°Ex
		9 osteoarthritis	Chronic	Physiotherapy, phenylbutazone	1	4	4	50°F → 55°F 160°Ex → 165°Ex
		1 gout	Chronic	Physiotherapy, Benemid	0	0	1	50°F → 40°F 150°Ex → 170°Ex

*N-none; M-moderate; E-excellent; F-flexion; Ex-extension; Abd-abduction.

A total of 56 patients were studied over a 6-month period. This included various forms of arthritis, bursitis, and post-traumatic lesions involving rheumatic structures.

RESULTS

A tabulation of results of therapy with hydrocortisone in concentrated form can be seen in Table I, where joint location, type of disease, duration of illness, prior therapy, and subjective and objective results are indicated. The over-all incidence of improvement is approximately similar to that reported in other series. However, the preponderance of chronic lesions and the unusually good results in certain locations usually more resistant to therapy, make the final evaluation slightly better than those reported. Success in some reported series indicates a favorable response for at least 3 days, which may not be sufficient either to satisfy the patient or to make continuation of therapy worth while.

No response in this series was reported when injection had no effect or only a transitory effect lasting 1 to 2 days. Moderate response was improvement for 3 to 10 days. Excellent response was recorded for improvement of over 10 days (usually about 21 days) or for complete remission.

TABLE II. COMPARISON OF CONCENTRATED HYDROCORTISONE WITH NONCONCENTRATED HYDROCORTISONE

DISEASE	NO. CASES	EFFICACY			DURATION OF EFFECT		
		CONCENTRATED HYDROCORTISONE SUPERIOR	EQUAL	NONCONCENTRATED HYDROCORTISONE SUPERIOR	CONCENTRATED HYDROCORTISONE SUPERIOR	EQUAL	NONCONCENTRATED HYDROCORTISONE SUPERIOR
Rheumatoid arthritis	19	14	4	1	7	10	2
Osteoarthritis	15	9	5	1	8	5	2
Bursitis	14	10	4	0	8	4	2
Traumatic lesions	6	5	1	0	3	2	1
Gout	1	1	0	0	1	0	0
Disc disease	1	1	0	0	1	0	0

Ankles have shown an 83 per cent response; all elbows were aided by therapy; shoulders showed a 73 per cent response; and knees showed an 87 per cent response. Other joints were not sufficient in number to make a percentage figure meaningful. Increases in range of motion have been given on an average basis for each group of cases. When a comparison is made between the usual hydrocortisone form (50 mg./c.c.) and the concentrated hydrocortisone (150 to 200 mg./c.c.) (Table II), it can readily be seen that the concentrated form is superior in both efficacy and duration of effect. The over-all difference is slightly less marked than that reported by Hollander for hydrocortisone TBA over hydrocortisone, but a more marked difference is seen here in certain resistant types

of lesions which may ultimately constitute the chief indications for the concentrated hydrocortisone, i.e., tenosynovitis, chronic bursitis of the shoulder and elbow, and post-traumatic lesions.

Table III indicates duration of effect by tabulating incidence of improvement lasting varying numbers of days rather than merely averaging days' duration for one drug versus another. It can be seen that the biggest difference is the larger number of cases (40 per cent) in the concentrated hydrocortisone group with improvement lasting 11 days or more. When we consider the cases lasting more than 3 weeks, a considerable difference between the drugs is apparent.

TABLE III. COMPARATIVE DURATION OF EFFECT

DRUGS	NO. OF		DURATION OF CLINICAL BENEFIT (DAYS)				
	PTS.	JOINTS	NONE	0–3	4–10	11–20	>21
Concentrated hydrocortisone (150 to 200 mg./c.c.)	55	78	4(7.3%)	6(10.9%)	23(41.8%)	11(20%)	11(20%)
Hydrocortisone (50 mg./c.c.)	52	69	5(9.6%)	3(5.8%)	28(53.8%)	14(26.9%)	2(3.8%)

TABLE IV. SIDE EFFECTS WITH CONCENTRATED HYDROCORTISONE

TYPE	NUMBER	PERCENTAGE
Local exacerbation	5	9.1
Infection	0	0
Systemic		
Cardiovascular	2	3.6
Gastrointestinal	0	0
Metabolic	2	3.6
Mental	0	0

The side effects are shown in Table IV. A significant percentage of local reactions is noted from the use of concentrated hydrocortisone, but reactions were not sufficiently marked to discontinue the injections except in one case. No infections were noted. Systemic effects included two cases developing transient edema for 24 hours after injection, one case of diabetes showing an increase in urinary sugar for 24 hours after injection, and one case demonstrating weight gain for one day. Other symptoms such as cardiovascular (elevated blood pressure, tachycardia), gastrointestinal (heartburn or epigastric distress), metabolic (hair or skin changes), or mental (mood changes) were absent in this series. Although hydrocortisone is absorbed in large part, there is apparently little systemic effect from a local dose of even 200 mg. Were the injections given daily or every other day, it is quite possible that more pronounced systemic effects would be present.

No significant differences between the 150 mg./c.c. and 200 mg./c.c. dosage forms were noted in efficacy, duration of effect, or incidence of side reactions. The slightly more frequent occurrence of needle blockage, when 200 mg./c.c. was used undiluted with procaine was the only difference noted.

In a few cases, an effect on noninjected joints was noted, and this effect was prolonged in some instances. This is understandable when we consider that a definite percentage of the locally injected steroid can be found in the contralateral joint.

In several of the cases of traumatic arthritis or bursitis, C-reactive protein determinations were made and, when found positive, were rechecked following hydrocortisone administration. In all joints or bursae responding to intra-articular therapy, the C-reactive protein became negative after 1 to 2 doses of the steroid.

Ultrasonic physiotherapy after preliminary administration of concentrated hydrocortisone was used in some of the cases of resistant disease, and further improvement was demonstrated. This combination therapy will be reported in a separate series.

Two instances of post-traumatic infection, not included in the tabulations, were treated with the combination of Neomycin and concentrated hydrocortisone. One patient was seen following trauma to a latent arthritic joint with subsequent infection, and the other one was seen following intra-articular administration of procaine at another center. Both infections involved knees and responded well to the combination therapy with no local or systemic toxic manifestations noted.

It is our opinion that this form of hydrocortisone deserves further study. It is apparently superior in efficacy and duration to the usual form of hydrocortisone and is specifically useful for certain types of resistant rheumatic processes.

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SUMMARY

1. A review of intra-articular therapy is presented with particular emphasis on mechanisms of action, types of compounds available, and previously reported results.

2. A comparison of a newer, more concentrated form of hydrocortisone and conventional hydrocortisone is made on a variety of rheumatic processes.

3. Results are expressed in terms of specific joint responses, both subjective and objective, and comparisons of efficacy and duration of effect are reported.

4. Minimal side effects are noted, and no significant systemic manifestations are observed.

5. This concentrated form of hydrocortisone appears somewhat superior to conventional dosage forms, especially for certain types of resistant rheumatic processes.

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Editorials

THE DRUG INDUSTRY AND AMERICAN MEDICINE

The pharmaceutical firms in this country have come to occupy an increasingly important place in the hierarchy of forces affecting the public health. Most of the new drugs introduced into medical practice each year, for example, are derived fairly directly from research and development programs of the drug houses rather than from nonindustrial research. The bulk of postgraduate education is in the hands of the pharmaceutical industry, since its "newspapers," "journals," television programs, movies, throwaways, "detail men," advertisements, etc., surely have more impact on the average practitioner than do postgraduate courses, medical meetings, and the massive but largely unread medical literature. In addition, a significant percentage of institutional drug research is currently being supported by grants from drug houses.

Most business concerns seem to agree that they cannot long afford a "public be damned" policy for pragmatic reasons. Often this fact becomes confused with, or transmuted into, the notion that the *raison d'être* of a business concern is to promote the public welfare. As has been ably pointed out elsewhere,[1] such a philosophy does not make much sense, since the stark realities of the economy dictate that a prerequisite to business existence is a ledger which reads in the black. It takes no Machiavellian spirit to argue that drug houses, like other industries, must primarily concern themselves with making profits, and that if there has to be a choice between chronic financial loss and sacrifice of some ideal, the drug house will either have to jettison the ideal or disappear from view. It is not suggested that it is impossible to make money *and* have ideals, nor that a firm will not occasionally prefer a minor or short-term financial loss to the cutting of some ethical corners. It merely seems desirable to clarify the major responsibility of any business firm, i.e., to earn money for its stockholders.

Because of the touchy nature of drug house "business"—the public health—one often detects among drug industry representatives the sentiment that pharmaceutical firms are automatically less dollar-oriented than other industries. One hears that it is only the "small" firm or the "unethical" one which will try to palm off a useless drug or soft-pedal toxicity data. One is also told, repeatedly, that "it doesn't pay" to market a worthless compound because the expense of introduction is great[2] and because the public will quickly discover the fraud and forever after tend to associate the particular manufacturer with tawdry practices.[3]

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Yet is this true? It is not difficult to think of drugs which were introduced as therapy for a condition which they in fact did not affect, which enjoyed great success temporarily, and which amply repaid the original investment involved in their production and promotion. Antihistamines as therapy for the common cold constitute a good example. There are almost certainly at present a number of "sedatives," "hypnotics," "tranquilizers," and "muscle relaxants" on the market which are almost inert and yet which are selling well and will probably continue to earn profits for some time. There are certain factors which predispose to such undeserved success. One is that the new drug be nontoxic. A drug which either produces serious untoward effects or produces minor untoward effects with some frequency is likely to have a short half-life in the market place of medical usage. Another factor predisposing to success is that there be available no effective standard drug against which doctors and patients can compare a new drug. A third factor is that the drug be allegedly useful for some disease or symptom which is hard to evaluate or has a high rate of spontaneous or placebo-induced remission. If all these conditions obtain, there is no reason why an inert medication, vigorously promoted, cannot survive for years on the market and earn both money and prestige for the manufacturer.

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Obviously there is a certain amount of discontent among physicians—particularly in university circles—about the drug houses. Pleadings and warnings are issued at the industry periodically.[3,4] One hears snide remarks about drug houses at medical rounds or meetings. Some investigators refuse to accept grants-in-aid from drug houses. Some medical schools even refuse graduation prizes offered by drug houses! I believe these various acts can be traced to several causes. First, there is a good deal of "aggressive" drug advertising[2] about claims that are poorly substantiated or therapeutic preparations whose use represents poor medical practice. Some of the antianemia preparations, tranquilizer mixtures, and antibiotic combinations are examples of this type of product. This is particularly frustrating because of the great tendency among American physicians to prescribe any new medication without any more information on its worth than what their "detail man" has told them. Second, although there are increasing numbers of drug house grants with no strings attached, many such grants-in-aid are naturally oriented around specific drugs in which the drug house or the investigator is interested. The manufacturers may not hold it against the investigator if he comes up with an unenthusiastic report, but they will certainly be happier if the reports are glowing. The manufacturer is also often anxious to have data as quickly as possible and may seem to the investigator to badger him repeatedly for reports. Some drug houses not only request that they be shown any articles to be published that have come out of such supported studies, but may try to alter the paper by bringing pressure to bear (usually subtly, sometimes crudely) on the author prior to publication. If the author desires further support from such a company, his position becomes most difficult. Finally, many physicians and educators resent the role the drug houses play in shaping medical practice via the various means described earlier in this paper. There is, for example, strong sentiment in many university departments against the practice of drug houses ordering 100,000 or more reprints of an article and

distributing such reprints to doctors throughout the country. Such practice seems to many to utilize an investigator's name or that of his institution in a fashion which is singularly queasy.

Are such frictions bad? It would seem so. One can assume that the American public (lay and professional) is interested in obtaining effective drugs and good therapy. It seems also reasonable to expect that the greatest advances in therapeutics will result from a pooling of the talents and resources of nonindustrial researchers and the pharmaceutical industry. Anything hampering this cooperation will impede medical progress. If large and influential segments of the medical profession withdraw still further from contact with and influence upon drug houses, the industry will lose the skills and criticisms of such men, and the profession will essentially abrogate a large part of its role in the evaluation of new drugs and postgraduate education. If industry does not face up to some of the mischief being perpetrated by some of its members, there may be professional or governmental pressure for reforms or restrictions which might prove inequitable or unwise. There are apparently some moves being made to sound out opinion on these problems.[2]

There is so much at stake for all concerned that it is to be hoped that both industry and the medical profession will approach the problem not only with open minds but with a sincere will to effect remedial changes. There is no advantage to be gained from stiff backs, holier-than-thou attitudes, defensive and aggressive postures on either side. There is much to be said for the special attitudes and viewpoints of the pharmaceutical industry and its critics but we will not improve matters by reciting a list of the good qualities of, and contributions made by, each side to medical progress. *What is being done wrong or left undone by both groups, and what can we do to change things for the better?*

There are some happy precedents which suggest ways for improving matters. The life insurance companies, with a high stake in improving the health of the public, have gained good will and contributed to the scientific scene by pooling resources and furnishing fellowships and grants-in-aid via the instrument of academic advisory boards who assign funds independent of pressure from donor firms. A similar, albeit much smaller, program has been operated for some years by the National Research Council through its Committee on Drug Addiction and Narcotics, with review of applications and disbursement of funds completely in the hands of a competent independent committee. Several drug houses here and abroad have established nonprofit research foundations for supporting investigators and institutions, with no relation whatsoever to drug products. The American Drug Manufacturers' Association has recently begun to foster the training of clinical pharmacologists by establishing training fellowships in university departments interested in such problems. On the academic side, there is also evidence of improved attitudes. It was not so many years ago that drug house employees, regardless of past achievements or current research activities, were automatically barred from membership in one of our learned societies. This form of "pharmaceutical Fifth Amendment" is, happily, no longer in use. Progress of the sort described cannot fail to improve relationships between industry and the medical profession and help bring these forces more closely to-

gether. Expansion of such programs and attitudes and the early elimination of certain unfortunate aspects of pharmaceutical practice will go far to allay the worries currently troubling not only the critics of industry but many of its friends.

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RETIREMENT PROBLEMS

During 1958, approximately half a million relatively "healthy" Americans will leave their jobs and enter retirement.

Today more than 14,000,000 men and women have reached the arbitrarily selected age of 65 which is used by most organizations as a basis for retirement. Their number is increasing at more than 400,000 a year. Another 100,000 or so will retire earlier voluntarily or because of relatively minor disabilities.

For some of those who will retire this year, 1958 will mean the achievement of a long-held dream of time for travel, hobbies, a new job, or a long-desired avocation. Unfortunately, they will be in the minority.

Retirement for the majority will be a difficult and unhappy period of readjustment with loss of needed income and a lowered standard of living.

A study made by the Twentieth Century Fund, published in 1956, showed that nearly three-fourths of all Americans over the age of 65 have either no income of their own or less than one thousand dollars a year. Only 15 per cent of the group have two thousand dollars or more.

Even among the group with more than two thousand dollars income a year or who will receive financial help from their children, the rosy picture of retirement they have held for years will not materialize, simply because they have not planned for it.

A large East Chicago company found that 80 per cent of its retired workers who moved to Florida, Arizona, and California returned to East Chicago. They could not find happiness away from friends, relatives, and familiar surroundings.

The most familiar complaint encountered among retired persons with financial security is, "I just don't have anything to do."

For a number of years, many communities have recognized the value of Golden Age, Senior Citizens, and similar organizations designed to provide either income-producing or leisure-time activities for older persons. More recently, however, communities and industry are recognizing that the time to solve "retirement problems" is before retirement. One group with an interesting experience with preretirement counseling is Harold R. Hall and Associates, Wellesley Hills, Mass.

Mr. Hall became interested in these problems while he was a member of the faculty of the Harvard Graduate School of Business Administration and discussed them in his book, *Some Observations on Executive Retirement.*

It was natural that when he himself retired, in 1953, he put his own theories to practice by becoming an independent consultant on retirement preparation. Since then he and his associates have worked with twenty-seven organizations

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Adapted from an article by Dr. Rusk which appeared in *The New York Times* on Sunday, January 26, 1958.

representing some of the nation's largest industries and businesses. Their program is in essence one of "help-you-to-help-yourself" through group meetings and subsequent personal interviews.

The program in a company begins with a series of group meetings starting with top management personnel and working down through the echelons of middle management through what is usually called the rank and file personnel. Usually group meetings are voluntary and are limited to twenty persons over 50 years of age.

In these group meetings about half of the time is spent in over-all discussion and the other half in discussion of actual cases of "before and after" retirement situations. At the end of the group meetings, participants are given a printed "Pattern for Exploration of Retirement Preparation" and are asked if they wish personal interviews.

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One interesting value to management of such retirement preparation programs is a subsequent strengthening among key personnel of desire to train their successors because they themselves have developed attractive alternatives of their jobs. This is in contrast to the letdown in the job interest that occurs with many employees a year or so before they retire.

Two studies among participants in the preretirement program showed that an overwhelming percentage believed the program had been helpful to them and was worth while. These favorable responses were higher among executive than nonexecutive personnel, but a large majority of the latter voluntarily expressed appreciation of management's interest in their welfare.

Although this need has been recognized recently, surprisingly little research has been done on the problems of retirement. One of the best publications of the subject is "Flexible Retirement," produced by the National Committee on Aging of the National Social Welfare Assembly and published by G. P. Putnam's Sons last year.

Another of the several organizations conducting preretirement consulting services is the Douglas Williams Associates, 342 Madison Avenue, New York, New York. The following are some of the interesting results this organization found in 864 responses to 1,740 questionnaires mailed to employees aged 54 to 65 of the Bell Telephone Company of Pennsylvania. (1) Only about half of those not yet retired felt that retirement would involve an easy readjustment; a vast majority of those who had already retired reported particular readjustment problems. (2) Only a few of the employees approaching retirement had definite plans for retirement, and less than one-third of those already retired had definite plans when they retired. (3) There is a much higher percentage of satisfaction among those already retired who had definite plans when they retired. (4) Among those who had retired, financial planning, how to occupy time, where to live, personal health, and living arrangements were considered the most important aspects of retirement which should be planned.

Some extremely useful material should result from the recently initiated study of the Department of Health, Education and Welfare, in which 3,000 newly retired persons will be asked to report over the next 12 years just how they get along in retirement.

The project is a part of a long-range study to provide more information about the circumstances encountered by Social Security beneficiaries in their later years. The questions will cover income, savings, housing, health, employment, major expenditures, and various activities of retired persons.

As one of the series of articles on the problems of aging which it is publishing for its Committee on Aging, the *Journal of the American Medical Association* published an article (165:15, 1957) on retirement by Mrs. Elizabeth Beckenridge. Mrs. Beckenridge is Supervisor of Services for the Aging of the Illinois Public Service Commission.

She summarized: "There has been ample evidence that programs of preparation for retirement serve to improve the quality of living for older people. The factual information they convey helps ward off many mistakes in budget planning and living arrangements and assists in creating an intelligent attitude toward personal health maintenance. Finally the actual process of looking clearly at the future usually is of great psychological value in reducing the apprehension and uncertainty about old age that haunts so many people.

"With the present and impending impact of a larger old age group on so many phases of American life, including its impact on medical care, it is folly not to work vigorously for the extension of these programs. In their conduct, the doctor can assume varying degrees of leadership, but it is essential that he cooperate wholeheartedly with the other organizations and professions in this unparalleled educational crusade."

The physician should be interested in retirement planning not only as an aid to his patients but as an aid to his own retirement. Some of these implications have been pointed out by E. Shanas and D. C. Gruen in their chapter "Means of Work for Older Physicians" in the book *Meaning of Work and Retirement* by E. A. Friedmann and R. J. Havighurst. (University of Chicago Press, 1954.)

Even though we may have retired from our jobs, each of us needs something to do that is purposeful and constructive. We live in a society that emphasizes that man's role is a creative and constructive one. Most of us have worked steadily and industriously in a society that respects only the productive. We have become accustomed to a certain amount of stress. This is the vital elixir of life. Regardless of age, it is essential in the proper dosage to the maintenance of health and happiness.

The stress that has stimulated us in our lifework must be replaced in retirement by the use of the "beneficent stress" that comes from new pursuits—vocational, avocational, educational, cultural, and recreational.

There is an adage "action absorbs anxiety." Applied to the individual who is preparing to retire, purposeful activity under the ceiling of stress not only absorbs anxiety but also prevents both physical and emotional deterioration.

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Book Reviews

AN INTRODUCTION TO THE STUDY OF EXPERIMENTAL MEDICINE. By Claude Bernard. Translated by Henry Copley Green, A.M., with an introduction by Lawrence J. Henderson, and a new foreword by I. Bernard Cohen. New York, 1957, Dover Publications, Inc. Pp. 226. Price $1.50.

Here, in an inexpensive but nicely printed and bound edition, is one classic that deserves wide reading. There is not enough of Bernard's work available in English, and for those who, like this reviewer, have read more *about* this great physiologist than *by* him, this new edition is a most happy event. Although Bernard is a bit repetitious and could have used a good editor, he has a lot to say and can turn a neat phrase when necessary. The following are some samples:

"If a comparison were required to express my idea of the science of life, I should say that it is a superb and dazzlingly lighted hall which may be reached only by passing through a long and ghastly kitchen."

"Man is by nature metaphysical and proud."

"Mathematical analysis becomes a blind instrument, if we do not from time to time retemper it in the furnace of experiment."

"Facts are neither great nor small in themselves. A great discovery is a fact whose appearance in science gives rise to shining ideas, whose light dispels many obscurities and shows us new paths."

". . . it is better to know nothing than to keep in mind fixed ideas based on theories whose confirmation we constantly seek, neglecting meanwhile everything that fails to agree with them."

". . . in nature what is absurd. . . is not always impossible."

"Great men . . . do not . . . respect the authority of their own predecessors, and they do not expect us to treat them otherwise."

"The words, life, death, health, disease, have no objective reality."

". . . to learn how man and animals live, we cannot avoid seeing great numbers of them die. . . ."

"Poisons are veritable reagents of life, extremely delicate instruments which dissect vital units."

". . . dead anatomy teaches nothing. . . ."

". . . there never are any unsuccessful experiments. . . ."

". . . criticism in every science must be done by men of science themselves, and by the most eminent masters."

"Experimenters do not grow great by the number and complexity of instruments."

"We must have robust faith and not believe."

The latter part of the book contains a partial review of some of the great experiments of Bernard, utilizing actual sequences to illustrate principles. This giant's ingenuity, breadth of interest, and contributions to physiology are in full evidence in this book, which is highly recommended.

Louis Lasagna

THE RELATION OF PSYCHIATRY TO PHARMACOLOGY. By Abraham Wikler, M.D. Published for the American Society for Pharmacology and Experimental Therapeutics by the Williams and Wilkins Co., Baltimore, 1957. Pp. 322, indexed. Price $4.00.

Dr. Wikler is an extraordinary person—neurophysiologist, pharmacologist, psychiatrist, philosopher—and he has written an extraordinary book. It is a superb review of a tremendous amount of diverse literature from the fields of clinical and experimental psychology and psychiatry, pharmacology, neurophysiology, and biochemistry. There are only a handful of people in the world who could even tackle such an awesome task, let alone produce a classic monograph. This is not the first such contribution Dr. Wikler has made; it is a pleasure to be once more in his debt. Bravo!

Louis Lasagna

ARTERIAL EMBOLISM. By John M. Askey, M.D. New York, 1957, Grune and Stratton, Inc. Pp. 138; indexed. Price $5.75.

This is an excellent book. There is a bibliography of 281 references on various aspects of the thromboembolism problem. This extensive literature has been critically reviewed and the information presented in usable form. The consideration of arterial embolism in patients with rheumatic heart disease is worthy of study by physicians concerned with the management of such patients. The influence of the type of cardiac rhythm and the type of valvular lesion on the probability of embolism is discussed, and the value of mitral valvulotomy as a prophylactic measure is clearly stated. The use of anticoagulants in the treatment of myocardial infarction is analyzed and sensible conclusions set forth. The author is a strong proponent of anticoagulant therapy on an outpatient basis, and his arguments are supported by convincing statistics. The reviewer's attitude toward the use of anticoagulants in both acute and chronic thromboembolic diseases has been changed significantly by this book.

Richard S. Ross

GENERAL DIAGNOSIS AND THERAPY OF SKIN DISEASES. By Hermann Werner Siemens, M.D. Translated by Kurt Wiener, M.D. Chicago, 1958, University of Chicago Press. Pp. 324; 375 illustrations; indexed. Price $10.00.

Over a period of years many very extensive textbooks of dermatology have been prepared. Most of these have run into many pages of reasonably small print, despite which it has seldom been possible for the authors to cover all of the essential points of diagnosis and treatment of skin diseases. One reason for this, perhaps, is that a great many words have been necessary to describe synonyms for extremely rare variations of the disorders in question. Another reason has been that, in general, more words are needed to describe disorders which are poorly understood. It is difficult to believe that there is a good short cut. In this relatively short book (310 pages) the author has chosen to discuss and to describe the morphology and distribution of skin lesions and to comment briefly upon therapy. Roughly two-thirds of this book is devoted to a minute description of skin lesions. The descriptions are accompanied, in most instances, by good photographs. Diagnostic pictures of various disorders are not drawn. Therapy as described by the author is made simple by restricting the formulary to a few basic vehicles. Few of the great number of active ingredients which may be added to these are considered. This simplification of the formulary has been expounded in most other recent texts.

To the reviewer, a neophyte in dermatology, the author's strong stand that there is seldom a relationship between disorders of the skin and systemic disorders was a shock. This philosophy is not expanded greatly in the book but seems to be stated quite clearly.

Altogether the book does not seem to add a great deal to the existing dermatologic literature and will probably not prove as useful to the student or to the dermatologist as a more encyclopedic type of book.

Ernest Smith

PRACTICAL NOTES ON NURSING PROCEDURES. By Jessie D. Britten, S.R.N. E. & S. Livingstone, Ltd., Edinburgh and London, 1957, Williams & Wilkins Co., Baltimore, Md. Pp. 192, indexed. Price: $4.00.

The usability of *Practical Notes on Nursing Procedures* is enhanced by the use of clear diagrams. More than one method of carrying out procedures is described. A separate chapter giving clear descriptions of laboratory examinations merits commendation. This little volume would offer little help to students of nursing in this country, as it is written for use in Great Britain and centers around equipment and procedures not utilized here.

Mary S. Price

PSYCHOPATHIC PERSONALITIES. By Harold Palmer, M.D. New York, 1957, Philosophical Library, Inc. Pp. 179. Price $4.75.

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This small volume consists of nine "clinical essays" concerning the clinical entities of schizophrenia, hysteria, depressive state, "psychopathic personalities," the obsessions, the epilepsies, the tension syndrome, the paranoid states, and mania. In the preface, the author explains that he has attempted primarily to present psychiatry in a way acceptable to workers in other fields.

Much space is devoted to a description of symptoms and constellations of personality characteristics, although the author does consider somewhat more briefly other important aspects of the patient, such as attitudes, motivations, and characteristic modes of interpersonal relationships. In this task, the author exhibits a refreshing freedom from doctrinaire bias, and at times his phraseology is pleasantly piquant. However, all too often, these qualities are obscured by a lack of cohesiveness, much repetitiveness, and a barrage of aphoristic phrases. These criticisms apply in particular to the chapters on psychopathic personalities, schizophrenia, and the tension syndrome. In the latter chapter, for example, the author cites Gillison in suggesting that in "highly strung" patients, "the ability to relax mentally and physically is the most important treatment."

There are some comments with which this reviewer would take sharp issue. For example, in discussing schizophrenics, the author states: ". . . . one never gets to know such people, equally it is true to say that there is very little to know about them or indeed worth knowing, outside the clinical field." Considering this position, it is no surprise that the very brief section on treatment is concerned principally with physical treatment and that psychotherapy is all but dismissed with the comment, "In all treatment of chronic schizophrenia, there is but one golden rule: the prevention of bad habit formation and the inculcation of good habit formation."

The essay on hysteria is interesting, and the chapter on the epilepsies is well worth reading. Considered as a whole, however, this book cannot be enthusiastically recommended to psychiatrists or to interested persons in other fields.

John B. Imboden

SCIENTIFIC WRITING. By Meta Riley Emberger and Marian Ross Hall. New York, 1955, Harcourt, Brace and Company. Pp. 468, indexed. Price $4.50.

The major fault with this book is the authors' attempt to cover too much ground. The result is a rather specious treatment of such massive topics as scientific method, research problems, terminology, and principles of logic, combined with a generally sketchy handling of the content suggested in the book's title. Perhaps the most interesting parts of the book are the many fine quotations, culled from an amazing variety of sources. The authors have obviously read widely, but I do not think they have written a book that will be terribly useful to scientific writers.

Louis Lasagna

HORMONES IN BLOOD. Vol. 11 of Ciba Foundation Colloquia on Endocrinology. Edited by G. E. Wolstenholme and E. C. P. Millar. Boston, 1957, Little, Brown and Co. Pp. 416, indexed. 74 illustrations. Price $9.00.

The English Ciba Colloquia are, I suppose, quite similar in most ways to our Macy Conferences. Yet the English symposia usually seem a good deal meatier and less diffuse. Whether this is due to the personnel involved, the sequence of formal paper-discussion-general discussion, or other factors, I do not know. In any case, the present volume will contain much of interest to endocrinologically-minded folk and is recommended to them. Other readers will probably find the going pretty rough, since the chairman himself says that ". . . this (colloqium) has I think been the least intelligible to the general biologist."

Louis Lasagna

DRUGS AND THE MIND. By Robert S. de Ropp, Ph.D. St. Martin's Press, New York 1957. Pp. 310, indexed. Price $4.50.

This book is devoted to a variety of drugs employed therapeutically or illicitly to alter the state of the central nervous system. It resembles closely a book written some years ago by Norman Taylor entitled *Flight From Reality*. The style is aimed primarily at the layman and makes for good reading. In many ways, de Ropp has done a creditable job of wading through a large body of literature (much of it controversial) and ending up usually on the side of the angels. The early chapters on mescaline and marihuana quote at length from the writings of famous figures who experimented with these drugs, and are of considerable interest. (It is fascinating, incidentally, in reading this book, to note how similar many of the experiences of such writers are, *regardless* of the drug involved.) The author is properly critical of much of the writing on opiates and of our cultural attitudes toward narcotic addicts. He shares this reviewer's minimal enthusiasm for De Quincey's *Confessions of an Opium Eater*. When de Ropp comes to the tranquilizing drugs, however, he seems perhaps unduly optimistic about the results of treatment with such agents and has given rather short shrift to the unenthusiastic reports.

It is unfortunate that intermingled with so much satisfactory medical journalism there should be such painful features as the careless spelling of drug names ("Pentathol," "Trapazole," "Azacyclonal," e.g.) and errors of fact (such as equating methadon and Dilaudid).

Nevertheless, it would appear that the book is a reasonably adequate popular treatment of an important area of pharmacology. The lay public and many physicians should enjoy this volume.

Louis Lasagna

PRACTICAL USE OF THE OFFICE LABORATORY AND X-RAY. By Paul Williamson, M.D. St. Louis, 1957, The C. V. Mosby Company. Pp. 323; indexed. Price $10.75.

This slim but ambitious volume seems to have been written for the young practitioner who might find it convenient to have in one book an introduction to office laboratory methods. The author's skeptical approach to the laboratory is wholesome, and his emphasis is on the indications for a particular test and on errors in its execution and interpretation—so much so that the book is somewhat short on methodology. There are undoubtedly a number of helpful hints, but the author's chatty discoursive style, garnished with unsupported statements that must have been fun to write but hair-raising to read, makes it unwise to recommend the book. If the recent medical school graduate, for whom this book is intended, does not already know the material in this volume and its errors, then our medical schools are doing a poor job. On the other hand, the physician might find it useful to give this book to his laboratory technician for the good advice it offers on the role of the laboratory.

Kenneth L. Zierler

Announcements

Dr. Donal Sheehan, dean of New York University College of Medicine, has announced a $5,000 one-year fellowship given anonymously to the department of physical medicine and rehabilitation. The fellowship, effective July 1, will provide training for a physician specializing in rehabilitation of the aged and will be given on the geriatric rehabilitation service in New York City's Goldwater Memorial Hospital on Welfare Island.

Dr. Michael M. Dacso is director of the 90-bed service which provides rehabilitation for disabled patients over 60 years old. This is one of a number of rehabilitation services in New York and neighboring hospitals maintained by the department of physical medicine and rehabilitation. Dr. Howard A. Rusk is professor and chairman of the department and director of the Institute of Physical Medicine and Rehabilitation of New York University-Bellevue Medical Center.

Increased stipends for its international trainees within the department of physical medicine and rehabilitation of New York University College of Medicine have been announced by Dr. Donal Sheehan, dean, and Dr. Howard A. Rusk, professor and chairman of the department. This increase is effective July 1 and will cover all current and future international trainees.

There are now 55 international trainees (47 physicians and 8 nonphysicians) from 27 nations participating in advanced and basic training in the medical speciality of physical medicine and rehabilitation, physical therapy, occupational therapy, social work, and prosthetics in the affiliated teaching institutions of the department. The department bears direct professional responsibility for physical medicine and rehabilitation clinical services at New York University-Bellevue Medical Center's Institute of Physical Medicine and Rehabilitation and University Hospital, The Bellevue Hospital Center, and Goldwater Memorial Hospital, which also has a Geriatrics Rehabilitation Service and the Regional Respirator and Rehabilitation Center.

Additional clinical facilities affiliated for teaching purposes include Elmhurst General Hospital; Hospital for Joint Diseases; St. Vincent's Hospital; New York Veterans Administration Hospital (Manhattan); St. Barnabas Hospital; Montefiore Hospital; Beekman-Downtown Hospital; Grasslands Hospital (Valhalla, N. Y.); New York State Rehabilitation Hospital (West Haverstraw, N. Y.); Henry Ford Hospital (Detroit, Mich.); Kessler Institute for Rehabilitation (West Orange, N. J.); and the Children's Seashore House (Atlantic City, N. J.).

Under the new stipends, international trainees will be paid an additional minimum maintenance of $125 per month. Trainees not receiving maintenance will receive $250. All trainees with dependents will get an additional $300 per year for each dependent accompanying the trainee to the United States.

The Gerontological Society, Inc., will hold its eleventh annual scientific meeting at the Bellevue Stratford Hotel, Philadelphia, Pennsylvania, November 6, 7, and 8, 1958. The plan of the meeting is to serve as a particular source of information in each section in addition to general sessions for the comprehensive information of all students of gerontology.

Abstracts of papers for the program should be submitted to the Program Committee for consideration by July 1, 1958. Abstracts should be sent to the following sub-chairmen of the section in which the authors elect to give their papers.

Clinical Medicine: Dr. Ewald Busse, Duke University Hospital, Durham, North Carolina.
Biology: Dr. Morris Rockstein, Department of Physiology, New York University, 550 First Avenue, New York 16, New York.
Psychology: Dr. Ethel Shanas, National Opinion Research Center, 5711 South Woodlawn Avenue, Chicago, Illinois.
Sociology: Dr. W. M. Beattie, Jr., Department of Sociology, Washington University, St. Louis, Missouri.

Exact details of length of presentation and place on the program will be made available by the appropriate sub-chairmen. Scientific and commercial exhibits are scheduled with a series of social functions and a meeting open to the public. Chairman of the Exhibitions Committee is Dr. Leo Gitman, 813 Howard Avenue, Brooklyn 12, New York.

Co-chairmen of the meeting are: Dr. Warren Andrew, Bowman Gray School of Medicine, Winston-Salem, North Carolina; and Dr. Joseph T. Freeman, 1530 Locust Street, Philadelphia 2, Pennsylvania.

The National Association for the Prevention of Tuberculosis Commonwealth Chest Conference will hold its inaugural meeting Tuesday, July 1, at the Royal Festival Hall in London. Her Royal Highness the Duchess of Kent, President of the NAPT, will be present to open the conference.

Thirty-five countries will be represented at the conference, the scope of which will be much wider than in the past. The activities of the NAPT have been extended to cover diseases of the chest and heart. The program will include discussions on the prevention of tuberculosis and other chest diseases—including lung cancer, bronchitis, and pneumoconiosis—and on the latest clinical developments in treatment. Other sessions will deal with the welfare and rehabilitation of the patient and his family.

The speakers will include some of the foremost authorities from many parts of the world, and visitors from all countries are welcome, although Commonwealth problems will be given special emphasis.

An extensive exhibition to be held in the foyers of the Royal Festival Hall during the conference will illustrate, among other things, the modern drugs and equipment used in the preventive treatment of chest diseases. Manufacturers of pharmaceutical products, x-ray apparatus and photographic materials, surgical instruments, and hospital equipment will be staging special exhibits.

Visits to hospitals and clinics and tours of general interest will be arranged during the three days immediately following the sessions.

For further information, contact the Secretary-General, NAPT, Tavistock House North, Tavistock Square, London WC1.